

## EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	169154	phospholipid distearoylphosphatidylethanolamine (polyoxypropylene or polyoxyethylene).	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2007/06/21 12:13
L2	662	phospholipid distearoylphosphatidylethanolamine (polyoxypropylene or polyoxyethylene)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	AND	ON	2007/06/21 12:13
L3	18	phospholipid (succinyl distearoylphosphatidylethan olamine or distearoylphosphatidylethanolamine) (polyoxypropylene or polyoxyethylene) monomethyl	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	AND	ON	2007/06/21 12:16
L4	662	phospholipid (succinyl distearoylphosphatidylethan olamine or distearoylphosphatidylethanolamine) (polyoxypropylene or polyoxyethylene)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	AND	ON	2007/06/21 12:17
L5	23635	lipid membrane (pharmaceutical or medicament) surfactant	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	AND	ON	2007/06/21 12:18
L6	643	I5 and I4	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	AND	ON	2007/06/21 12:18
L7	17	I3 and I5	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	AND	ON	2007/06/21 12:20
L8	0	("1999313828") or ("1998085969").PN.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/06/21 12:21

## EAST Search History

L9	0	(("19990313828") or ("1998085969")).PN.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/06/21 12:21
L10	0	(("19990313828") or ("19980085969")).PN.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/06/21 12:21
L11	0	(("199900313828") or ("19980085969")).PN.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/06/21 12:21
L12	0	(("1999313828") or ("199885969")).PN.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/06/21 12:21
L13	2	("2002147136").PN.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/06/21 12:21
L14	2	("20020147136").PN.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/06/21 12:22
L15	2	("20020071843").PN.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/06/21 12:22
L16	3	("2002071843").PN.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/06/21 12:23

## EAST Search History

L17	2	("20020147136").PN.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/06/21 12:23
L18	3	("2002036161").PN.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/06/21 12:23
L19	2	("20020036161").PN.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/06/21 12:24
L20	1	("200236161").PN.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/06/21 12:25
L21	2	("6139819").PN.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/06/21 12:25
L22	0	("1996012353").PN.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/06/21 12:26
L23	3	("9731624").PN.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/06/21 12:26
L24	2	("5554728").PN.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/06/21 12:26

## EAST Search History

L25	2	("0307175").PN.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/06/21 12:27
L26	4	("4423038").PN.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/06/21 12:28
L27	0	("200384576").PN.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/06/21 12:28
L28	0	("200384574").PN.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/06/21 12:28
L29	4	("2003084574").PN.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/06/21 12:28
L30	3	(("2003440201") or ("2002360821")).PN.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/06/21 12:29
L31	0	(("20030440201") or ("20020360821")).PN.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/06/21 12:29
L32	0	(("200300440201") or ("200200360821")).PN.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/06/21 12:29

## EAST Search History

L33	2	("5614214").PN.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/06/21 12:30
L34	4	("9611670").PN.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/06/21 12:30
L35	41	I13 I14 I15 I16 I17 I18 I19 I20 I21 I23 I24 I25 I26 I29 I30 I33 I34	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2007/06/21 12:32
L36	1	I35 and I7	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2007/06/21 12:33
L37	2	I35 and I6	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2007/06/21 12:35
L38	0	"1997932273"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2007/06/21 12:36
L39	0	"19970932273"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2007/06/21 12:36
L40	0	"199700932273"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2007/06/21 12:36

JC 6/21/07  
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NEWS 2 MAR 15 WPIDS/WPIX enhanced with new FRAGHITSTR display format  
NEWS 3 MAR 16 CASREACT coverage extended  
NEWS 4 MAR 20 MARPAT now updated daily  
NEWS 5 MAR 22 LWPI reloaded  
NEWS 6 MAR 30 RDISCLOSURE reloaded with enhancements  
NEWS 7 APR 02 JICST-EPLUS removed from database clusters and STN  
NEWS 8 APR 30 GENBANK reloaded and enhanced with Genome Project ID field  
NEWS 9 APR 30 CHEMCATS enhanced with 1.2 million new records  
NEWS 10 APR 30 CA/CAplus enhanced with 1870-1889 U.S. patent records  
NEWS 11 APR 30 INPADOC replaced by INPADOCDB on STN  
NEWS 12 MAY 01 New CAS web site launched  
NEWS 13 MAY 08 CA/CAplus Indian patent publication number format defined  
NEWS 14 MAY 14 RDISCLOSURE on STN Easy enhanced with new search and display fields  
NEWS 15 MAY 21 BIOSIS reloaded and enhanced with archival data  
NEWS 16 MAY 21 TOXCENTER enhanced with BIOSIS reload  
NEWS 17 MAY 21 CA/CAplus enhanced with additional kind codes for German patents  
NEWS 18 MAY 22 CA/CAplus enhanced with IPC reclassification in Japanese patents  
NEWS 19 JUN 18 CA/CAplus to be enhanced with pre-1967 CAS Registry Numbers  
  
NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.  
  
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FILE 'HOME' ENTERED AT 10:51:51 ON 21 JUN 2007

=> file registry  
COST IN U.S. DOLLARS  
FULL ESTIMATED COST

SINCE FILE ENTRY	TOTAL SESSION
0.21	0.21

FILE 'REGISTRY' ENTERED AT 10:52:08 ON 21 JUN 2007  
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=>  
Uploading C:\Documents and Settings\jcho2\My Documents\10549630-i.str

L1 STRUCTURE uploaded

=> file registry	SINCE FILE ENTRY	TOTAL SESSION
COST IN U.S. DOLLARS		
FULL ESTIMATED COST	2.25	2.46

FILE 'REGISTRY' ENTERED AT 10:55:01 ON 21 JUN 2007  
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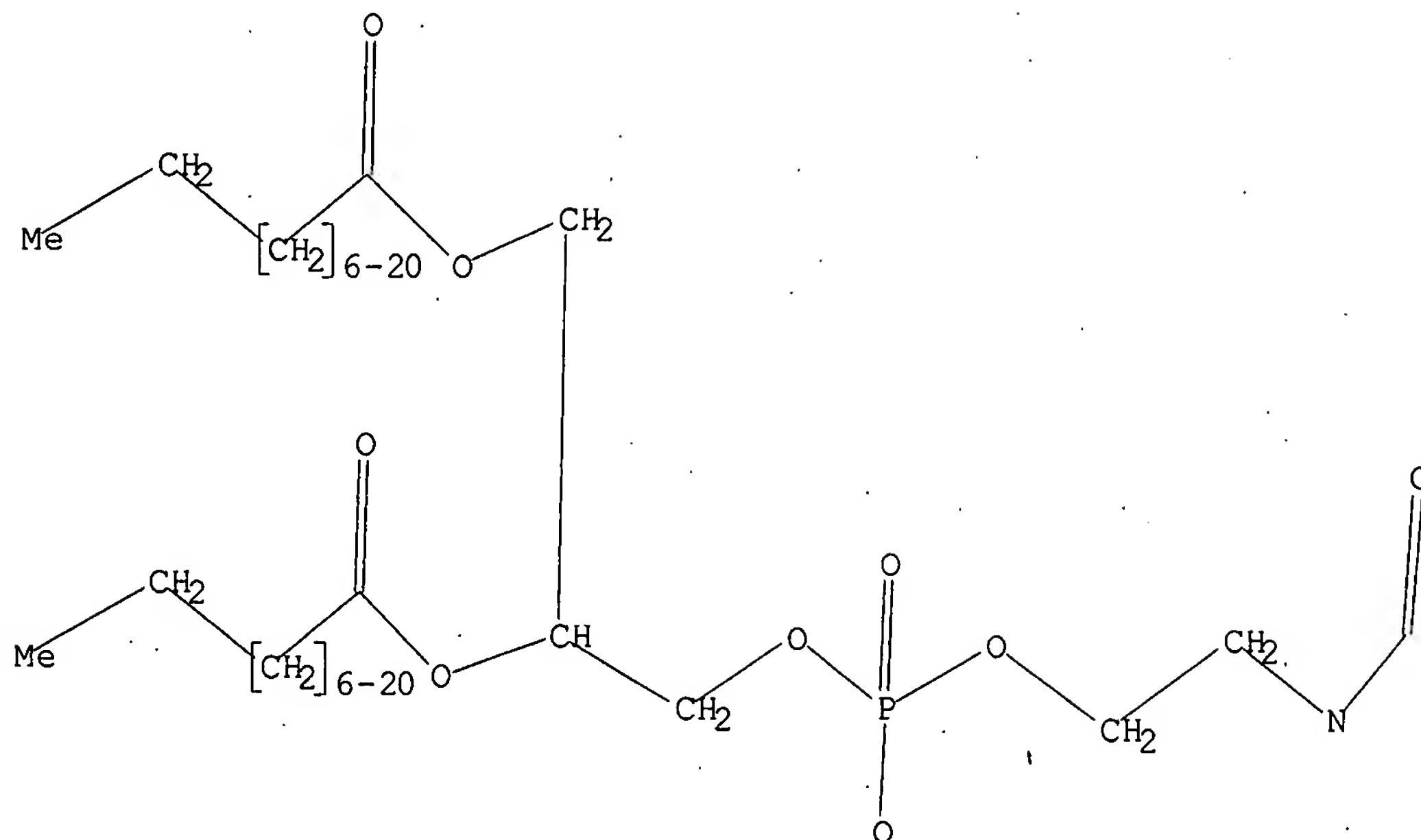
=>  
Uploading C:\Documents and Settings\jcho2\My Documents\10549630-j.str

L2 STRUCTURE UPLOADED

=> d 12

L2 HAS NO ANSWERS

L2 STR



Structure attributes must be viewed using STN Express query preparation.

=> s 12 sss full

FULL SEARCH INITIATED 10:55:41 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 3227 TO ITERATE

100.0% PROCESSED 3227 ITERATIONS

1113 ANSWERS

SEARCH TIME: 00.00.01

L3 1113 SEA SSS FUL L2

=> d scan

L3 1113 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN Poly(oxy-1,2-ethanediyl), α-[6-hydroxy-6-oxido-1,12-dioxo-9-[(1-oxooctadecyl)oxy]-5,7,11-trioxa-2-aza-6-phosphonacos-1-yl]-ω-hydroxy-, 8-ether with L-tyrosyl-D-alanyl-L-phenylalanylglycyl-L-tyrosyl-L-prolyl-L-seryl-S-[1-[3-[(2-hydroxyethyl)amino]-3-oxopropyl]-2,5-dioxo-3-pyrrolidinyl]-L-cysteine (9CI)

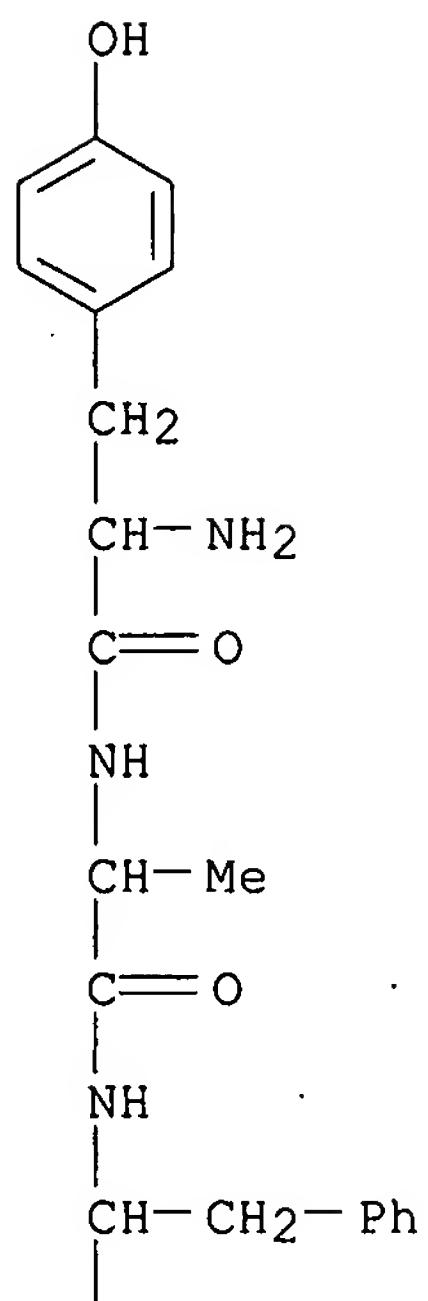
SQL 8

MF (C<sub>2</sub> H<sub>4</sub> O)<sub>n</sub> C<sub>94</sub> H<sub>146</sub> N<sub>11</sub> O<sub>25</sub> P S

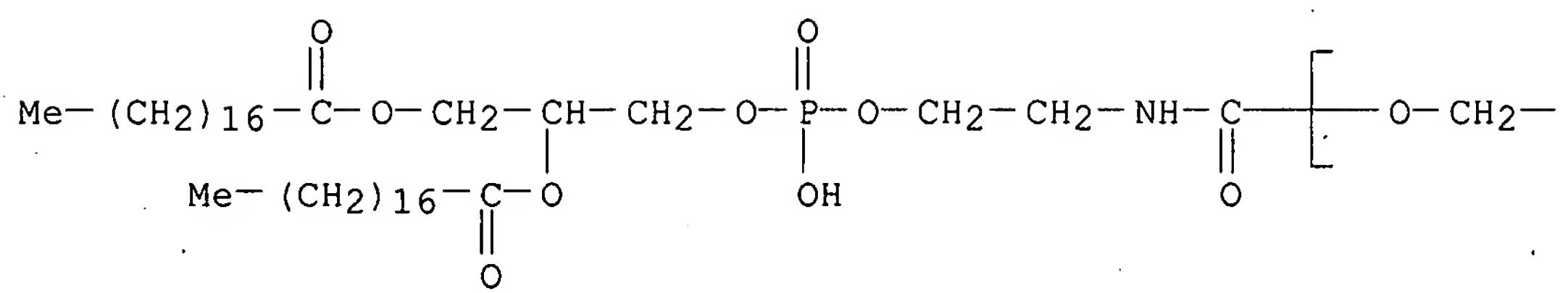
CI PMS

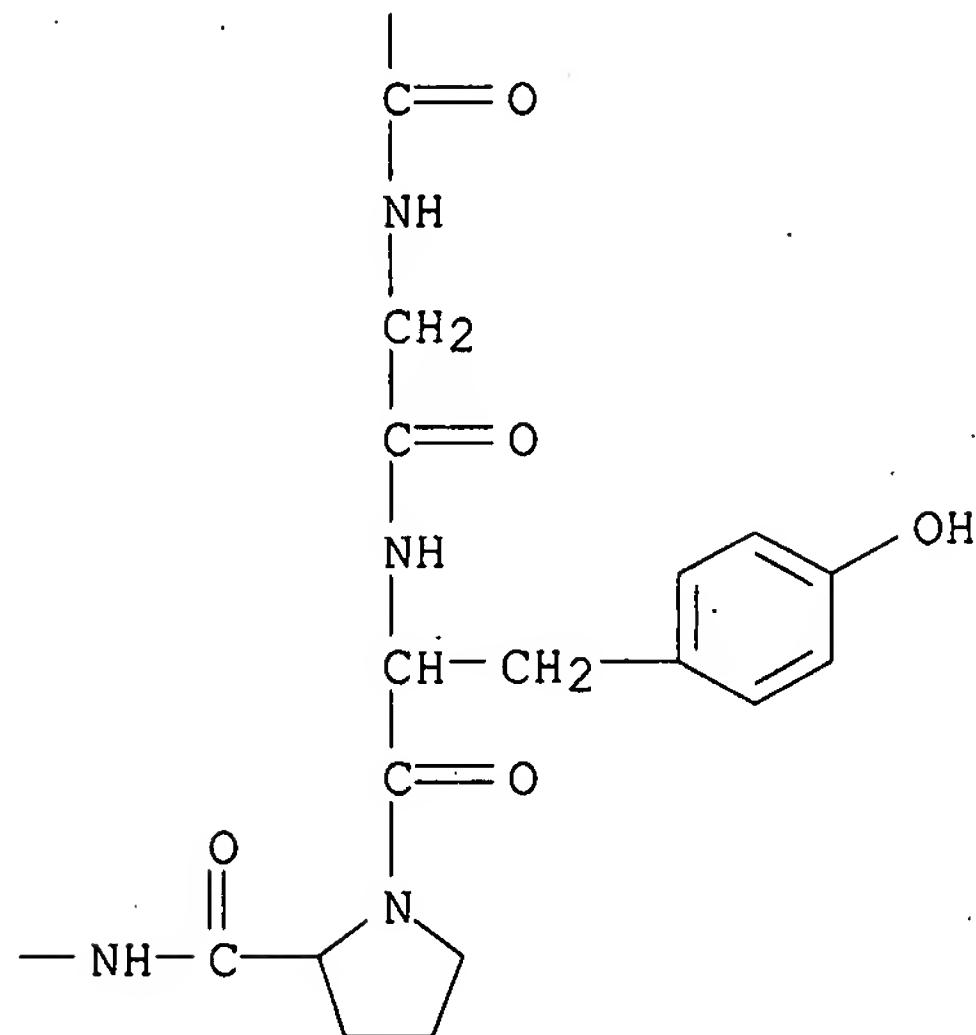
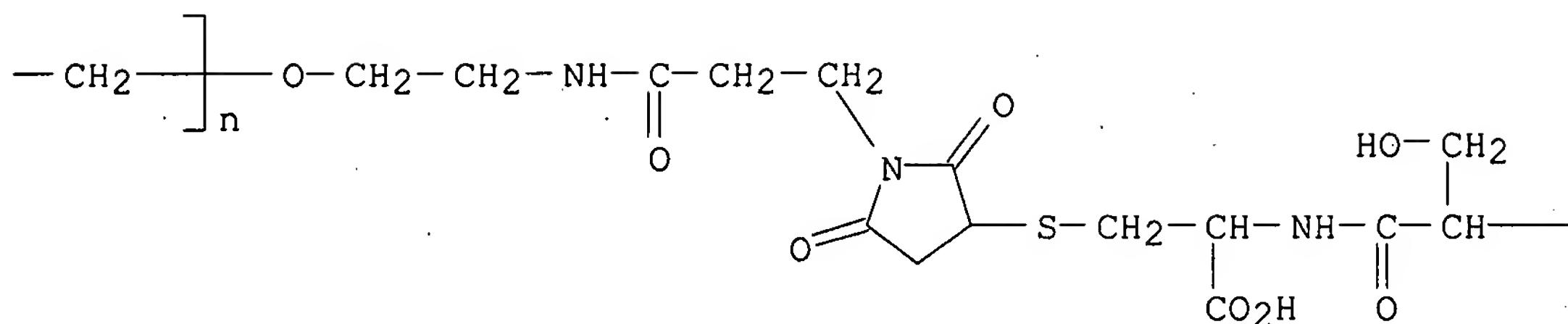
\*\*RELATED SEQUENCES AVAILABLE WITH SEQLINK\*\*

PAGE 1-C



PAGE 2-A





HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):end

=> file caplus  
COST IN U.S. DOLLARS  
FULL ESTIMATED COST

SINCE FILE ENTRY	TOTAL SESSION
172.55	175.01

FILE 'CAPLUS' ENTERED AT 10:56:13 ON 21 JUN 2007  
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=> s 13  
L4 1068 L3

=> log off  
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF  
LOGOFF? (Y)/N/HOLD:n

=> file registry  
COST IN U.S. DOLLARS SINCE FILE TOTAL  
ENTRY SESSION  
FULL ESTIMATED COST 3.29 178.30

FILE 'REGISTRY' ENTERED AT 11:00:34 ON 21 JUN 2007  
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=>  
Uploading C:\Documents and Settings\jcho2\My Documents\10549630-k.str  
L5 STRUCTURE uploaded

=> d 15  
L5 HAS NO ANSWERS  
L5 STR

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

Structure attributes must be viewed using STN Express query preparation.

=> s 15 sss full  
FULL SEARCH INITIATED 11:01:20 FILE 'REGISTRY'  
FULL SCREEN SEARCH COMPLETED - 365 TO ITERATE

100.0% PROCESSED 365 ITERATIONS  
SEARCH TIME: 00.00.01

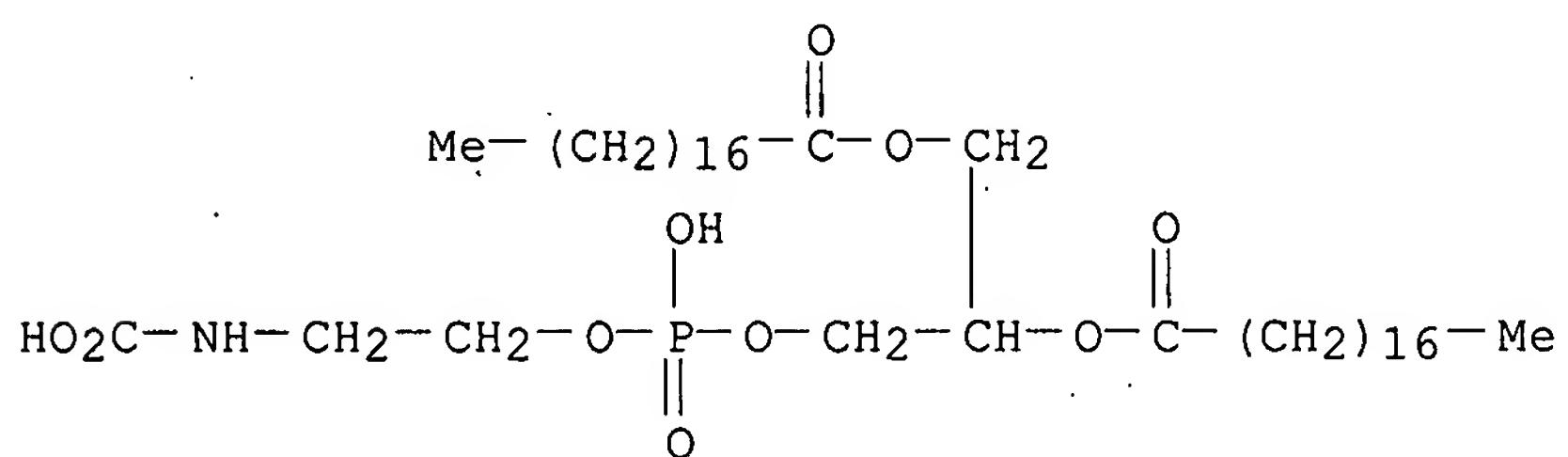
2 ANSWERS

L6 2 SEA SSS FUL L5

=> d scan

L6 2 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN  
IN Oxirane, methyl-, polymer with oxirane, mono[6-hydroxy-6-oxido-12-oxo-9-[(1-oxooctadecyl)oxy]-5,7,11-trioxa-2-aza-6-phosphonacosanoate], methyl ether (9CI)  
MF C42 H82 N O10 P . (C3 H6 O . C2 H4 O)x . C H4 O

CM 1

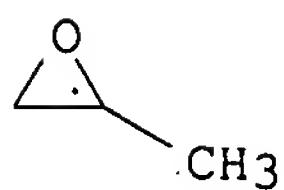


CM 2

H<sub>3</sub>C-OH

CM 3

CM 4



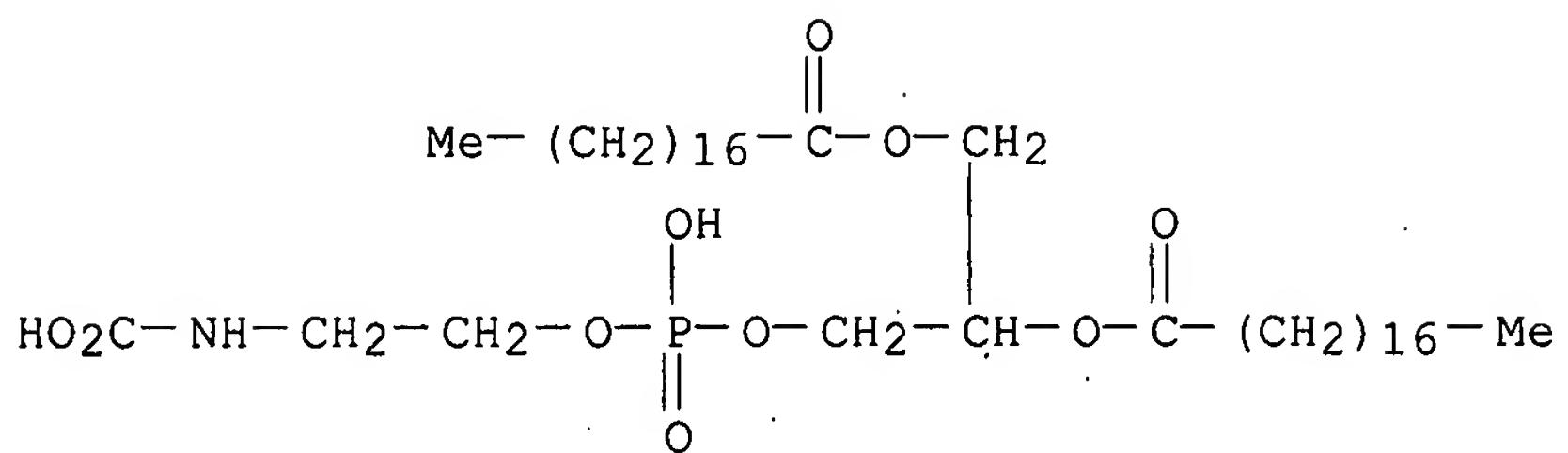
CM 5



HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):2

L6 2 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN  
IN 5,7,11-Trioxa-2-aza-6-phosphonacosanoic acid, 6-hydroxy-12-oxo-9-[(1-

oxooctadecyl)oxy]-, 6-oxide (9CI)  
MF C42 H82 N O10 P  
CI COM



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

ALL ANSWERS HAVE BEEN SCANNED

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=> s 16  
L7 1 L6

=> d 17 bib abs hitstr

L7 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS on STN  
AN 2004:799592 CAPLUS  
DN 141:320053  
TI Phospholipid derivatives for liposome compositions  
IN Itoh, Chika; Ohhashi, Syunsuke; Kubo, Kazuhiro; Yasukohchi, Tohru;  
Kikuchi, Hiroshi; Suzuki, Norio; Kurosawa, Miho; Yamauchi, Hitoshi  
PA NOF Corporation, Japan; Daiichi Pharmaceutical Co. Ltd.

SO . PCT Int. Appl., 39 pp.

CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 1

PATENT NO.		KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004083219	A1	20040930	WO 2004-JP3789	20040319
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG.				
US	2007031481	A1	20070208	US 2006-549630	20060817
PRAT	JP 2003-77242	A	20030320		

AB A phospholipid derivative represented by the formula  
R<sub>1</sub>COCH<sub>2</sub>CH(OCR<sub>2</sub>)CH<sub>2</sub>OP(OX)O<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>NHCO(CH<sub>2</sub>)<sub>a</sub>(CO)bO(A<sub>1</sub>O)<sub>m</sub>(A<sub>2</sub>O)<sub>n</sub>(A<sub>3</sub>O)<sub>q</sub>R<sub>3</sub>  
(R<sub>1</sub>CO, R<sub>2</sub>CO = acyl; R<sub>3</sub> = H, hydrocarbon; a = 0-4; b = 0-1, provided that when a is 0, then b is 0; X = H, alkali metal, ammonium, organic ammonium; A<sub>1</sub>O, A<sub>2</sub>O, and A<sub>3</sub>O = oxyalkylene; provided that the proportion of oxyethylene in A<sub>1</sub>O and A<sub>3</sub>O is 0.5 or higher by weight; and m, n, and q each indicates the average number of moles added, provided that 5 ≤ m ≤ 600, 1 ≤ n ≤ 45, 0 ≤ q ≤ 200, 10 ≤ m + n + q ≤ 600, 0.04 ≤ n/(m + n + q), and q/(m + n + q) ≤ 0.8). The derivative, on the surface of a liposome, is inhibited from spreading its polyalkylene oxide structure and thus serves to increase the amount of the hydrated layer on the surface and thereby heighten the stability of the liposome. A phospholipid compound monomethyl polyoxypropylene-polyoxyethylenesuccinyl distearoylphosphatidylethanolamine was prepared. The phospholipid 1.04 mM was mixed with hydrogenated soybean phosphatidylcholine (HSPC) 11.28 cholesterol 7.68 mM, and doxorubicin solution g.s. to form a liposome with an average particle size of 95 nm.

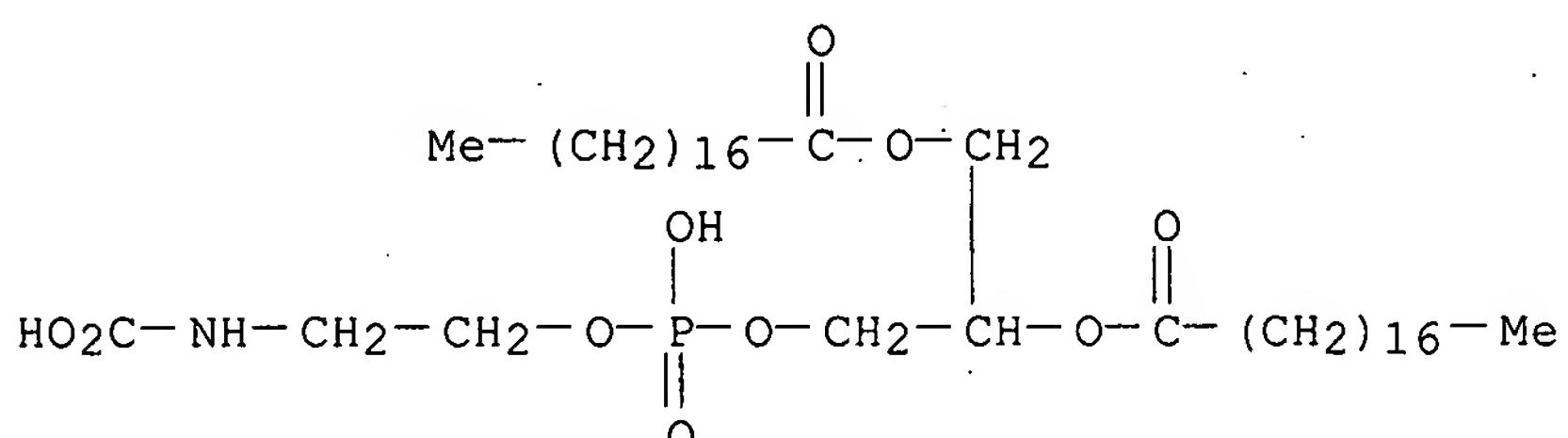
IT . 766509-45-9P, Monomethyl polyoxypropylene-polyoxyethylene  
carbamyl distearoylphosphatidylethanolamine  
RL: COS (Cosmetic use); SPN (Synthetic preparation); THU (Therapeutic  
use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(phospholipid derivs. for liposome compns.)

RN 766509-45-9 CAPLUS  
CN Oxirane, methyl-, polymer with oxirane, mono[6-hydroxy-6-oxido-12-oxo-9-[(1-oxooctadecyl)oxy]-5,7,11-trioxa-2-aza-6-phosphonacosanoate], methyl ether (9CI) (CA INDEX NAME)

CM 1

CRN 766509-44-8

CMF C42 H82 N 010 P



CM 2

CRN 67-56-1  
CMF C H4 O

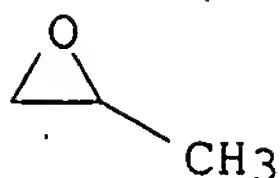
H<sub>3</sub>C-OH

CM 3

CRN 9003-11-6  
CMF (C<sub>3</sub> H<sub>6</sub> O . C<sub>2</sub> H<sub>4</sub> O) x  
CCI PMS

CM 4

CRN 75-56-9  
CMF C<sub>3</sub> H<sub>6</sub> O



CM 5

CRN 75-21-8  
CMF C<sub>2</sub> H<sub>4</sub> O



=> file registry  
COST IN U.S. DOLLARS

SINCE FILE ENTRY	TOTAL SESSION
7.62	358.47

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE ENTRY	TOTAL SESSION
-0.78	-0.78

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DICTIONARY FILE UPDATES: 20 JUN 2007 HIGHEST RN 938114-25-1

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<http://www.cas.org/support/stngen/stndoc/properties.html>

=>

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L8 STRUCTURE UPLOADED

=> d 18

L8 HAS NO ANSWERS

L8 STR

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

Structure attributes must be viewed using STN Express query preparation.

=> s 18 sss full

FULL SEARCH INITIATED 11:05:32 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 1078 TO ITERATE

100.0% PROCESSED 1078 ITERATIONS  
SEARCH TIME: 00.00.01

L9 18 SEA SSS FUL L8

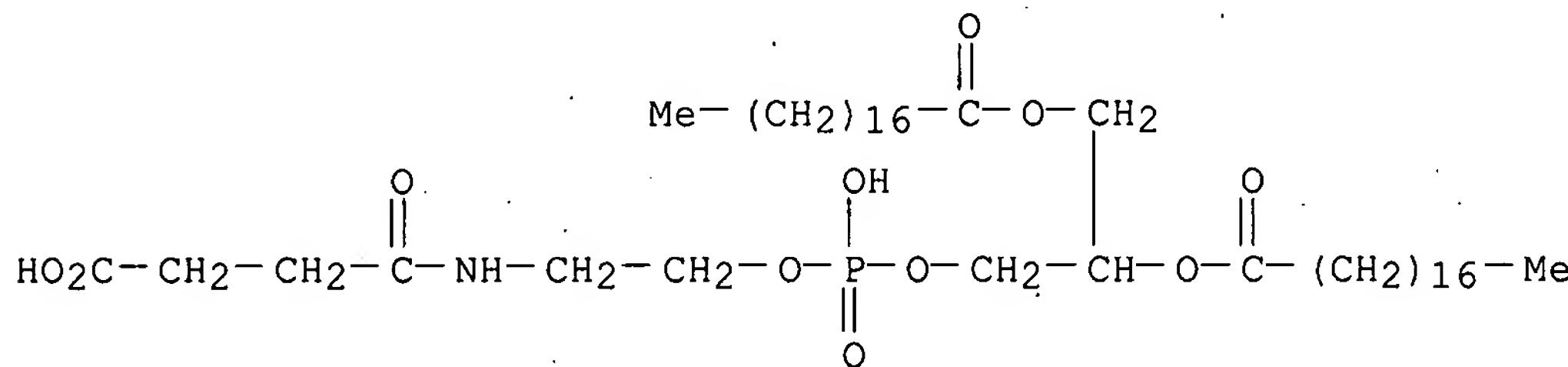
=> d scan

L9 18 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 1,2,3-Propanetriol, homopolymer, mono[9-hydroxy-9-oxido-4,15-dioxo-12-[(1-oxooctadecyl)oxy]-8,10,14-trioxa-5-aza-9-phosphadotriacontanoate] (9CI)

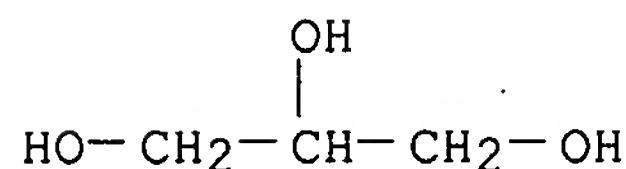
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CM 1



CM 2

CM 3



HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):end

=> file caplus  
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	172.55	531.02

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-0.78

FILE 'CAPLUS' ENTERED AT 11:05:46 ON 21 JUN 2007  
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FILE LAST UPDATED: 20 Jun 2007 (20070620/ED)

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<http://www.cas.org/infopolicy.html>

=> s 19  
L10 30 L9

=> d 110 1-30 bib abs hitstr

L10 ANSWER 1 OF 30 CAPLUS COPYRIGHT 2007 ACS on STN  
AN 2007:173633 CAPLUS  
DN 146:269771  
TI Separation processes  
IN Rongved, Pal; Loevhaug, Dagfinn; Fjerdingga, Hege; Solbakken, Magne;  
Godal, Aslak; Cuthbertson, Alan  
PA Norway  
SO U.S. Pat. Appl. Publ., 17pp., Cont.-in-part of U.S. Ser. No. 722,075.  
CODEN: USXXCO  
DT Patent  
LA English  
FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2007036722	A1	20070215	US 2006-498651	20060803
	CN 1234742	A	19991110	CN 1997-199047	19971028
	HU 9904595	A2	20000428	HU 1999-4595	19971028
	AT 318618	T	20060315	AT 1997-910514	19971028
	ES 2264159	T3	20061216	ES 1997-910514	19971028
	US 6261537	B1	20010717	US 1997-960054	19971029
	EP 1442751	A1	20040804	EP 2004-7226	19980424

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, FI, CY

ES	2224379	T3	20050301	ES	1998-917461	19980424
KR	2000052829	A	20000825	KR	1999-703658	19990427
US	2002102215	A1	20020801	US	2001-765614	20010122
US	2002102217	A1	20020801	US	2001-925715	20010810
US	6680047	B2	20040120			
CN	1440816	A	20030910	CN	2002-160420	20021230
US	2004141922	A1	20040722	US	2003-722075	20031126
US	2005002865	A1	20050106	US	2003-734730	20031215
PRAI	GB 1996-22366	A	19961028			
	GB 1996-22367	A	19961028			
	GB 1996-22368	A	19961028			
	GB 1997-699	A	19970115			
	GB 1997-8265	A	19970424			
	GB 1997-11842	A	19970606			
	GB 1997-11846	A	19970606			
	US 1997-49264P	P	19970606			
	US 1997-49265P	P	19970606			
	US 1997-49268P	P	19970606			
	US 1997-958993	A2	19971028			
	US 1997-960054	A1	19971029			
	US 2001-765614	B1	20010122			
	US 2003-722075	A2	20031126			
	GB 1996-22369	A	19961028			
	GB 1997-2195	A	19970204			
	GB 1997-11837	A	19970606			
	GB 1997-11839	A	19970606			
	US 1997-49263P	P	19970607			
	US 1997-49266P	P	19970607			
	US 1997-959206	A	19971028			
	EP 1998-917461	A3	19980424			
	US 2001-925715	A1	20010810			

AB Separation of target material from a liquid sample is achieved by coupling the target to targetable encapsulated gas microbubbles, allowing the microbubbles and coupled target to float to the surface of the sample to form a floating microbubble/target layer, and separating this layer from the sample. In a pos. separation process the microbubbles are then removed from the target, e.g. by bursting. In a neg. separation process target-free sample material is recovered following separation of the floating layer. The method may also be used diagnostically to detect the presence of a disease marker in a sample. Novel separation apparatus is also described. Gas microbubbles encapsulated with DSPS and thiolated anti-CD34 antibodies-Mal-PEG2000DSPE, useful for separation of hematopoietic stem cells, were prepared

IT 248253-94-3

RL: RCT (Reactant); RACT (Reactant or reagent)  
(in preparation of microbubbles carrying nitrilotriacetic acid chelate  
binding groups; separation processes and separation apparatus using

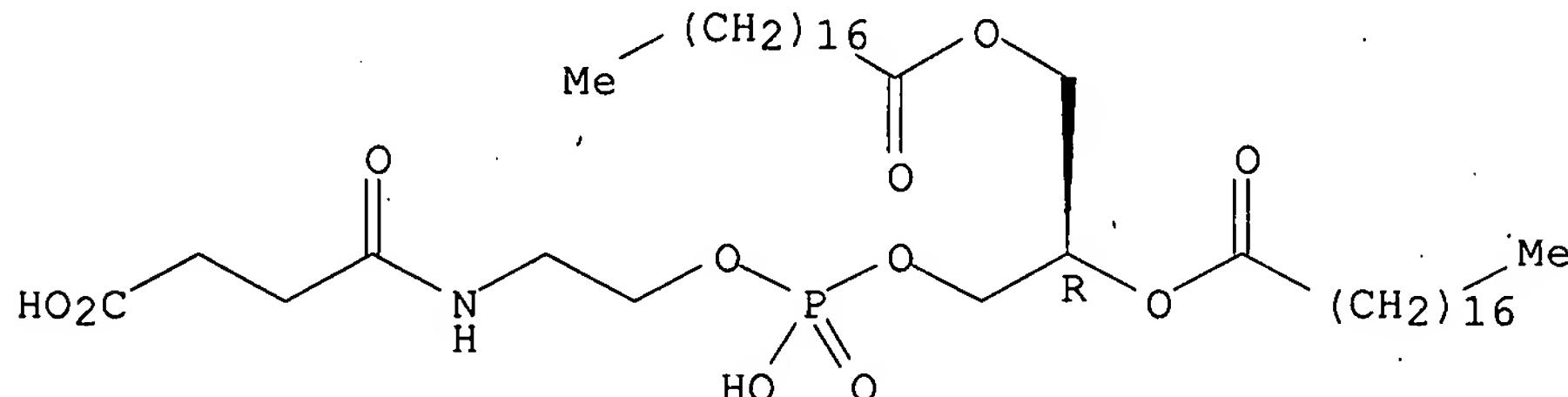
targetable

encapsulated gas microbubbles)

RN 248253-94-3 CAPLUS

CN 8,10,14-Trioxa-5-aza-9-phosphadotriacontanoic acid, 9-hydroxy-4,15-dioxo-12-[(1-oxooctadecyl)oxy]-, 9-oxide, (12R)- (CA INDEX NAME)

## Absolute stereochemistry.



L10 ANSWER 2 OF 30 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2006:1250986 CAPLUS

DN 146:33006

TI Lipid construct for delivery of insulin to a mammal

IN Lau, John R.; Geho, W. Blair

PA SDG, Inc., USA

SO PCT Int. Appl., 148pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006127361	A2	20061130	WO 2006-US19119	20060516
	WO 2006127361	A3	20070524		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
	US 2006222697	A1	20061005	US 2006-384659	20060320
	US 2006222698	A1	20061005	US 2006-384728	20060320
PRAI	US 2005-683878P	P	20050523		
	US 2006-384659	A	20060320		
	US 2006-384728	A	20060320		
	US 1998-85969P	P	19980519		
	US 1999-313828	A2	19990518		

AB The instant invention is drawn to a hepatocyte targeted composition comprising insulin associated with a lipid construct comprising an amphipathic lipid and an extended amphipathic lipid that targets the construct to a receptor displayed by an hepatocyte. The composition can comprise a mixture of free insulin and insulin associated with the complex. The composition can be modified

to protect insulin and the complex from degradation. The invention also includes methods for the manufacture of the composition and loading insulin into the composition and recycling various components of the composition. Methods of treating

individuals inflicted with diabetes are described. Thus, hepatic directed vesicle (HDV) insulin test materials were prepared containing about 191 ng/kg of

extended amphipathic lipid (Biotin-X DHPE or Biotin DHPE) and about 14.5 mg/kg of amphipathic lipids (a mixture of 1,2-distearoyl-sn-glycero-3-phosphocholine, cholesterol, and dicetyl phosphate). The test materials obtained had higher levels of hepatic glycogen in diabetic rats than did the regular insulin.

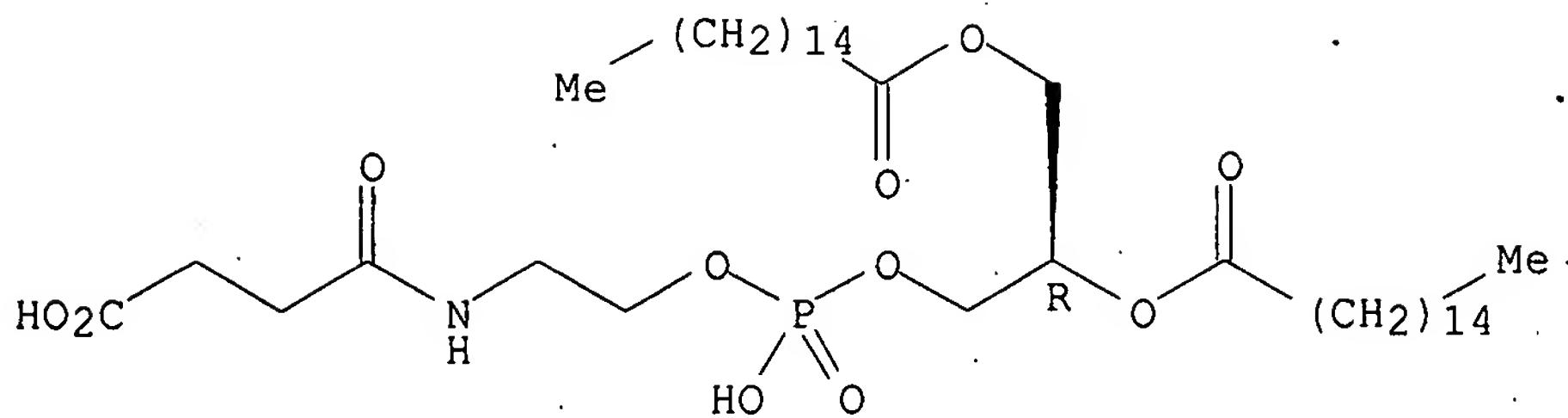
IT 150525-42-1

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(lipid constructs for insulin targeting to hepatocyte receptor and treatment of diabetes)

RN 150525-42-1 CAPLUS

CN 8,10,14-Trioxa-5-aza-9-phosphatriacontanoic acid, 9-hydroxy-4,15-dioxo-12-[(1-oxohexadecyl)oxy]-, 9-oxide, (12R)- (CA INDEX NAME)

Absolute stereochemistry.



L10 ANSWER 3 OF 30 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2006:1250980 CAPLUS

DN 146:50261

TI Lipid construct for delivery of interferon to a mammal

IN Lau, John R.; Geho, W. Blair

PA SDG, Inc., USA

SO PCT Int. Appl., 102pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006127360	A2	20061130	WO 2006-US19118	20060516
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRAI US 2005-683878P P 20050523

US 2006-384575 A 20060320

AB The instant invention is drawn to a hepatocyte targeted composition comprising interferon associated with a lipid construct comprising amphipathic lipid mols. and receptor binding mol. The composition can comprise a mixture of free interferon and interferon associated with the complex. The composition can be modified to protect interferon and the complex from degradation. The invention also includes methods for the manufacture of the composition and loading

interferon

into the composition and recycling various components of the composition and methods

of treating individuals infected with the hepatitis C and other hepatitis viruses. For example, a lipid construct containing interferon  $\alpha$  was prepared from a mixture of the amphipathic lipids and an extended amphipathic lipid, i.e., 2-distearoyl-sn-glycero-3-phosphocholine, cholesterol, dicetyl phosphate, 1,2-dipalmitoyl-sn-glycero-3-phosphoethanolamine-N-(Cap Biotinyl), 1,2-distearoyl-sn-glycero-3-phosphoethanolamine, 1,2-dipalmitoyl-sn-glycero-3-phosphoethanolamine-N-(succinyl) and 1,2-dipalmitoyl-sn-glycero-3-[phospho-rac-(1-glycerol)] (sodium salt). The efficacy of the lipid construct, i.e., a hepatic directed vehicle (HDV) interferon  $\alpha$  (100  $\mu$ g HDV + 10  $\mu$ g interferon  $\alpha$ ) was evaluated in a mouse model. The interferon-stimulated response of the induction of the double stranded RNA dependent protein kinase (PKR) gene was used as a marker of interferon hepatic tissue delivery. Interferon alone provided approx. a 5-fold increase in PKR activation relative to a baseline. HDV-interferon  $\alpha$  provided approx. a 15-fold increase in

PKR activation relative to a baseline and approx. a 3-fold increase relative to interferon alone. Thus, interferon activity in the hepatic tissue was enhanced by delivering the interferon with HDV.

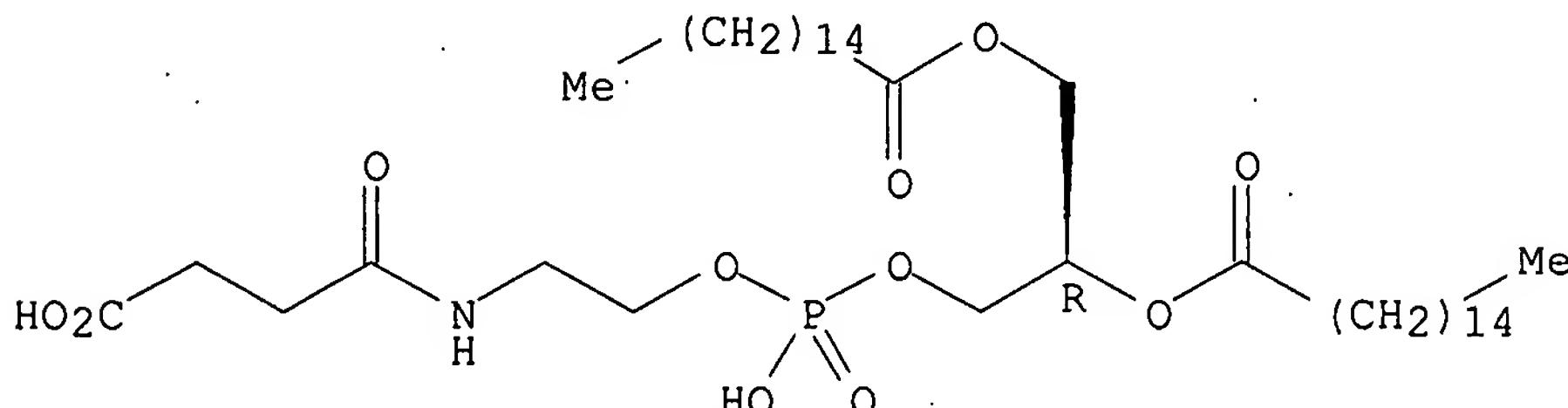
IT 150525-42-1

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (lipid constructs for interferon targeting to hepatocyte receptors and treatment of hepatitis)

RN 150525-42-1 CAPLUS

CN 8,10,14-Trioxa-5-aza-9-phosphatricontanoic acid, 9-hydroxy-4,15-dioxo-12-[(1-oxohexadecyl)oxy]-, 9-oxide, (12R)- (CA INDEX NAME)

Absolute stereochemistry.



L10 ANSWER 4 OF 30 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2006:681369 CAPLUS

DN 145:146029

TI Preparation of peptide-containing compounds for targeting cells expressing NP-1 receptor

IN Von Wronski, Mathew A.; Marinelli, Edmund R.; Nunn, Adrian D.; Pillai, Radhakrishna; Ramalingam, Kondareddiar; Tweedle, Michael F.; Linder, Karen E.; Nanjappan, Palaniappa; Raju, Natarajan

PA Bracco International B.V., Neth.

SO U.S. Pat. Appl. Publ., 98 pp., Cont.-in-part of Ser. No. US 2001-871974, CODEN: USXXCO

DT Patent

LA English

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2006153775	A1	20060713	US 2006-342050	20060127
	US 2002147136	A1	20021010	US 2001-871974	20010604
	US 7109167	B2	20060919		
PRAI	US 2000-585364	B2	20000602		
	US 2001-871974	A2	20010604		

OS MARPAT 145:146029

AB The invention provides compds. for targeting endothelial cells, tumor cells or other cells that express the neuropilin-1 (NP-1) receptor, compns. containing the same and methods for their use. The compds. are of the formula A-L-B (A = a monomer, multimer or polymer of TKPPR or analog which specifically binds to NP-1 or cells expressing NP-1 with avidity equal or greater than TKPPR; L = a lipid or a non-lipid (e.g., polymer) linker; B = a substrate). Addnl., the present invention includes diagnostic, therapeutic and radio-therapeutic compns. useful for visualization, therapy or radiotherapy. For example, DPPE-glutaroyl-Gly-Thr-Lys-Pro-Pro-Arg-OH (DPPE-Glu-GTKPPR) was prepared and formulated into gas-filled microbubble compns. for ultrasonic echog. The bubbles bind to human aortic endothelial cells (HAEC) under flow. The number of bubbles bound may increase with time for several minutes at a given flow rate, up to a flow rate producing 1.53 dynes/cm<sup>2</sup>, while bubbles without the targeting moiety (DPPE-Glu-GTKPPR) may not bind. However, once bound under a lesser flow rate (e.g., 1.53 dynes/cm<sup>2</sup>), the shear stress on bubbles containing DPPE-Glu-GTKPPR may be increased to 6.1 dynes/cm<sup>2</sup> without dislodging many

of the bound bubbles.

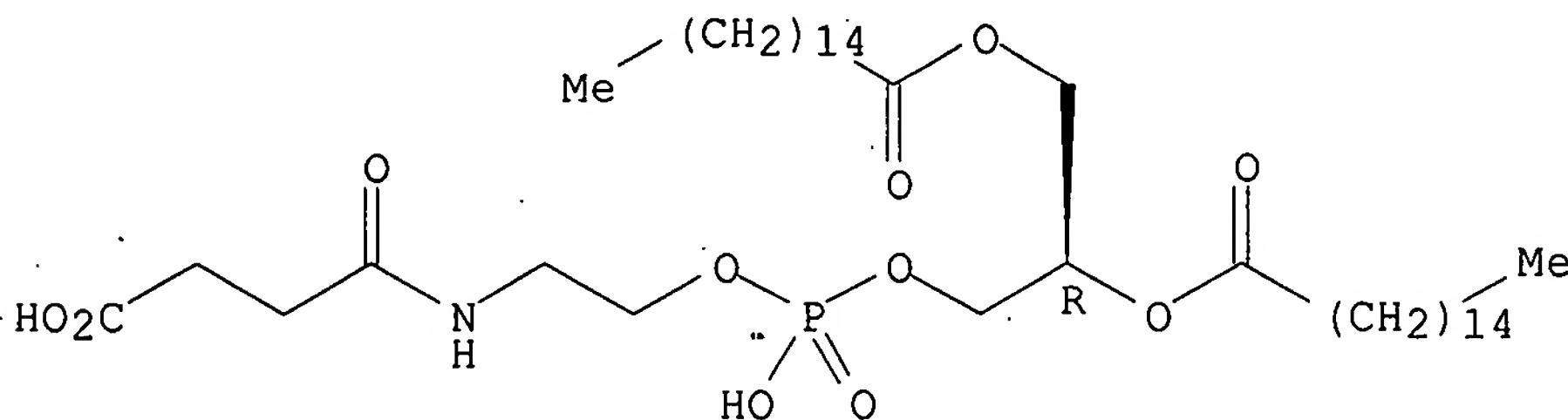
IT 150525-42-1P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of peptide-containing compds. and compns. for targeting cells expressing neuropilin-1 receptor for diagnosis, imaging, and therapy)

RN 150525-42-1 CAPLUS

CN 8,10,14-Trioxa-5-aza-9-phosphatetracontanoic acid, 9-hydroxy-4,15-dioxo-12-[(1-oxohexadecyl)oxy]-, 9-oxide, (12R)- (CA INDEX NAME)

Absolute stereochemistry.



L10 ANSWER 5 OF 30 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2005:492463 CAPLUS

DN 143:13409

TI Phospholipid membranes having allergen or antibodies on the surface

IN Uchida, Tetsuya; Mori, Masato

PA NOF Corporation, Japan; National Institute Infectious Diseases

SO Jpn. Kokai Tokkyo Koho, 28 pp.

CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 2005145959	A	20050609	JP 2004-305217	20041020
	US 2005266066	A1	20051201	US 2004-969543	20041020
PRAI	JP 2003-360047	A	20031020		

AB The invention relates to a phospholipid membrane consisting of C10-12 acyl or hydrocarbon group-containing phospholipids and a phospholipid membrane stabilizer, wherein the phospholipid has antibody or allergen on the surface. The antibody or allergen-bound phospholipid membrane is suitable for use in a liposome for hyposensitization therapy. Liposome was prepared from didodecanoylephosphatidylcholine, didodecanoylephosphatidylethanolamine, cholesterol, and didodecanoylephosphatidylserine sodium salt, and treated with ovalbumin to obtain ovalbumin-immobilized liposome. The obtained ovalbumin-immobilized liposome induced IgG in a mouse at a ratio IgE/IgG ≤ 0.001.

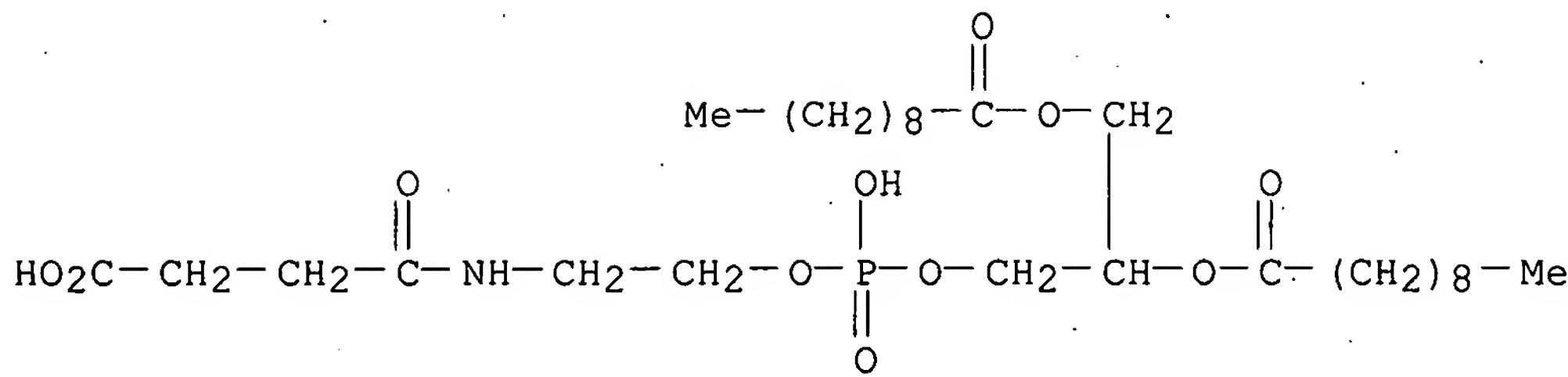
IT 852462-67-0P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(phospholipid membranes having allergen or antibodies on the surface suitable for use in liposomes)

RN 852462-67-0 CAPLUS

CN 8,10,14-Trioxa-5-aza-9-phosphatetracontanoic acid, 9-hydroxy-4,15-dioxo-12-[(1-oxodecyl)oxy]-, 9-oxide (9CI) (CA INDEX NAME)



L10 ANSWER 6 OF 30 CAPLUS COPYRIGHT 2007 ACS on STN  
AN 2005:453648 CAPLUS  
DN 143:13245  
TI Remote detection of substance delivery to cells  
IN Drummond, Daryl C.; Hong, Keelung; Kirpotin, Dmitri B.  
PA USA  
SO U.S. Pat. Appl. Publ., 31 pp.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2005112065	A1	20050526	US 2004-888794	20040709
	AU 2004264857	A1	20050224	AU 2004-264857	20040709
	WO 2005016141	A1	20050224	WO 2004-US22133	20040709
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRAI	US 2003-486080P	P	20030709		
	WO 2004-US22133	W	20040709		

AB The present invention provides for the development of endocytosis-sensitive probes, and a remote method for measuring cellular endocytosis. These probes are based on the reduced water permeability of a nanoparticle or liposomal delivery system, and inherent degradability or disruption of barrier integrity upon endocytosis. The invention also provides for liposomes having combined therapeutic and diagnostic utilities by co-encapsulating ionically coupled diagnostic and therapeutic agents, in one embodiment, by a method using anionic chelators to prepare electrochem. gradients for loading of amphipathic therapeutic bases into liposomes already encapsulating an imaging agent. The invention provides for imaging of therapeutic liposomes by inserting a lipopolymer anchored, remotely sensing reporter mols. into liposomal lipid layer. The invention allows for an integrated delivery system capable of imaging mol. fingerprints in diseased tissues, treatment, and treatment monitoring.

IT 248253-94-3P

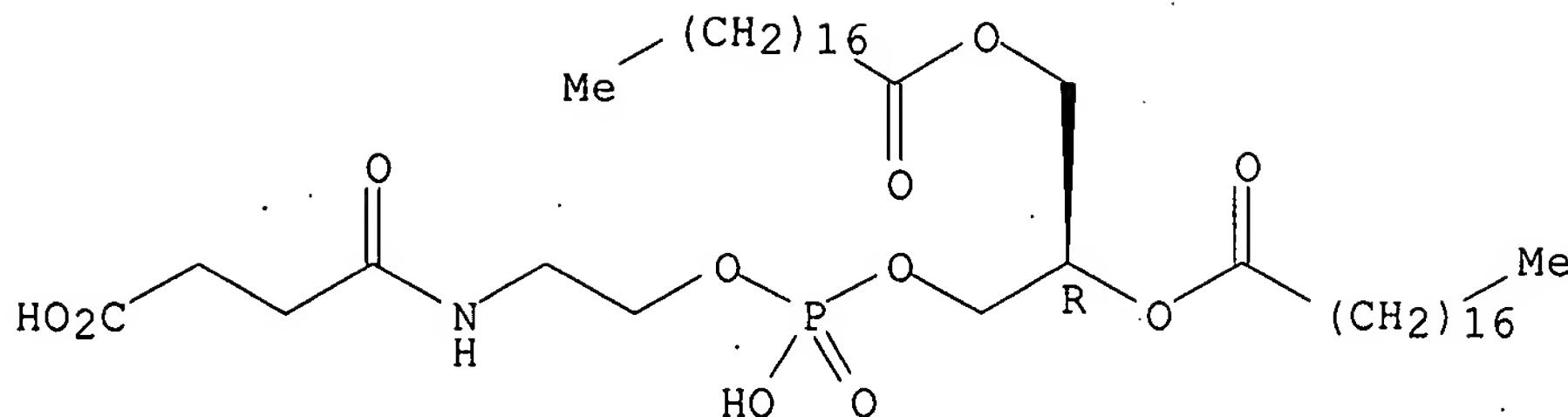
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(liposomal delivery systems as diagnostic and therapeutic agents)

RN 248253-94-3 CAPLUS

CN 8,10,14-Trioxa-5-aza-9-phosphadotriacontanoic acid, 9-hydroxy-4,15-dioxo-12-[(1-oxooctadecyl)oxy]-, 9-oxide, (12R)- (CA INDEX NAME)

Absolute stereochemistry.



L10 ANSWER 7 OF 30 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2004:861949 CAPLUS

DN 142:303393

TI Enhancement of the Efficacy of An Antagonist of an Extracellular Receptor by Attachment to the Surface of a Biocompatible Carrier

AU Wartchow, Charles A.; Alters, Susan E.; Garzone, Pamela D.; Li, Lingyun; Choi, Steven; DeChene, Neal E.; Doede, Tina; Huang, Linong; Pease, John S.; Shen, Zhimin; Knox, Susan J.; Cleland, Jeffrey L.

CS Targesome Inc., Palo Alto, CA, 94303, USA

SO Pharmaceutical Research (2004); 21(10), 1880-1885

CODEN: PHREEB; ISSN: 0724-8741

PB Springer Science+Business Media, Inc.

DT Journal

LA English

AB In order to improve the in vitro and in vivo efficacy of an integrin antagonist (IA) of the extracellular domain of the  $\alpha v \beta 3$  integrin, a receptor upregulated on tumor neovasculature, the IA was attached to the surface of a dextran-coated liposome (DCL). IA-DCLs were characterized in vitro, and the pharmacokinetic and anti-tumor properties were assessed in vivo. The in vitro binding properties were measured with purified integrin, endothelial cells, and melanoma cells. The pharmacokinetic parameters were measured in healthy mice with  $^{14}C$ -labeled IA-DCLs and anti-tumor efficacy was assessed with the M21 human melanoma xenograft mouse model. In vitro, IC<sub>50</sub> values for IA-DCLs and IA are similar, and IA-DCLs inhibit cell proliferation relative to controls. IA-DCLs are stable in serum, and the pharmacokinetic half-life in mice is 23 h. In the M21/mouse model, statistically significant inhibition of tumor growth was observed for mice treated with IA-DCLs, whereas controls including saline, DCLs lacking IA, and cyclo(RGDfV) were ineffective. Increased apoptosis and a reduction in vessel counts relative to controls were present in tumors from animals treated with IA-DCLs. These results demonstrate that IA-DCLs are potent anti-angiogenic therapeutic agents with superior in vivo activity and pharmacol. compared to unmodified IA.

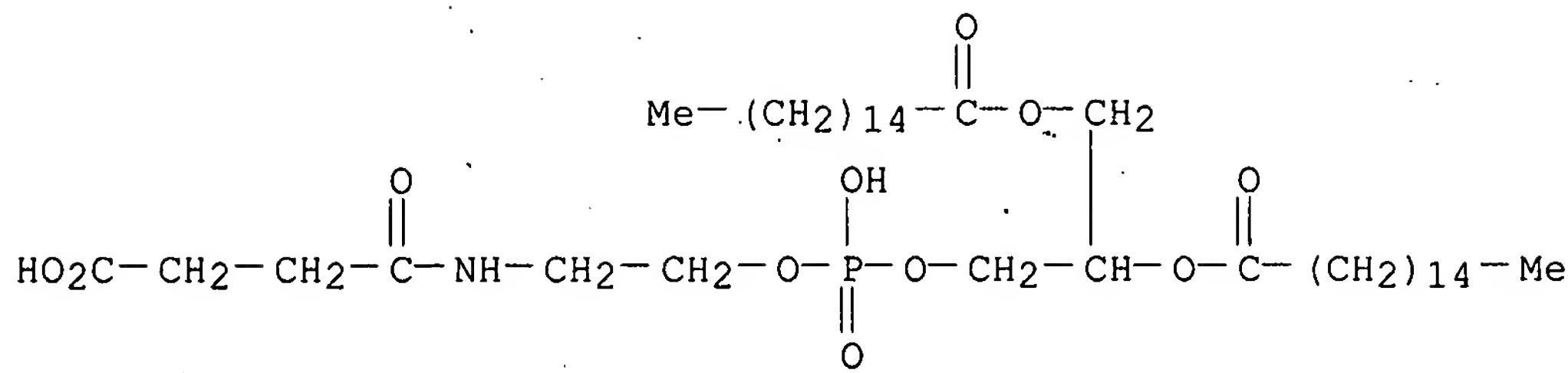
IT 88848-80-0

RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(enhancement of efficacy of an antagonist of an extracellular receptor by attachment to the surface of a biocompatible carrier)

RN 88848-80-0 CAPLUS

CN 8,10,14-Trioxa-5-aza-9-phosphatriacontanoic acid, 9-hydroxy-4,15-dioxo-12-[(1-oxohexadecyl)oxy]-, 9-oxide (9CI) (CA INDEX NAME)



RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 8 OF 30 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2004:799592 CAPLUS

DN 141:320053

TI Phospholipid derivatives for liposome compositions

IN Itoh, Chika; Ohhashi, Syunsuke; Kubo, Kazuhiro; Yasukohchi, Tohru;  
Kikuchi, Hiroshi; Suzuki, Norio; Kurosawa, Miho; Yamauchi, Hitoshi

PA NOF Corporation, Japan; Daiichi Pharmaceutical Co. Ltd.

SO PCT Int. Appl., 39 pp.

CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004083219	A1	20040930	WO 2004-JP3789	20040319
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2007031481	A1	20070208	US 2006-549630	20060817
PRAI	JP 2003-77242	A	20030320		
	WO 2004-JP3789	W	20040319		

AB A phospholipid derivative represented by the formula  
 $\text{R}_1\text{COCH}_2\text{CH}(\text{OCR}_2)\text{CH}_2\text{OP(OX)}\text{O}_2\text{CH}_2\text{CH}_2\text{NHCO(CH}_2)_a(\text{CO})_b\text{O}(\text{A}_1\text{O})^m(\text{A}_2\text{O})^n(\text{A}_3\text{O})^q\text{R}_3$   
(R<sub>1</sub>CO, R<sub>2</sub>CO = acyl; R<sub>3</sub> = H, hydrocarbon; a = 0-4; b = 0-1, provided that when a is 0, then b is 0; X = H, alkali metal, ammonium, organic ammonium; A<sub>1</sub>O, A<sub>2</sub>O, and A<sub>3</sub>O = oxyalkylene, provided that the proportion of oxyethylene in A<sub>1</sub>O and A<sub>3</sub>O is 0.5 or higher by weight; and m, n, and q each indicates the average number of moles added, provided that 5 ≤ m ≤ 600, 1 ≤ n ≤ 45, 0 ≤ q ≤ 200, 10 ≤ m + n + q ≤ 600, 0.04 ≤ n/(m + n + q), and q/(m + n + q) ≤ 0.8). The derivative, on the surface of a liposome, is inhibited from spreading its polyalkylene oxide structure and thus serves to increase the amount of the hydrated layer on the surface and thereby heighten the stability of the liposome. A phospholipid compound monomethyl polyoxypropylene-polyoxyethylenesuccinyl distearoylphosphatidylethanolamine was prepared. The phospholipid 1.04 mM was mixed with hydrogenated soybean phosphatidylcholine (HSPC) 11.28 cholesterol 7.68 mM, and doxorubicin solution q.s. to form a liposome with an average particle size of 95 nm.

IT 766509-39-1P, Monomethyl polyoxypropylene-polyoxyethylene succinyl distearoylphosphatidylethanolamine  
RL: COS (Cosmetic use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(phospholipid derivs. for liposome compns.)

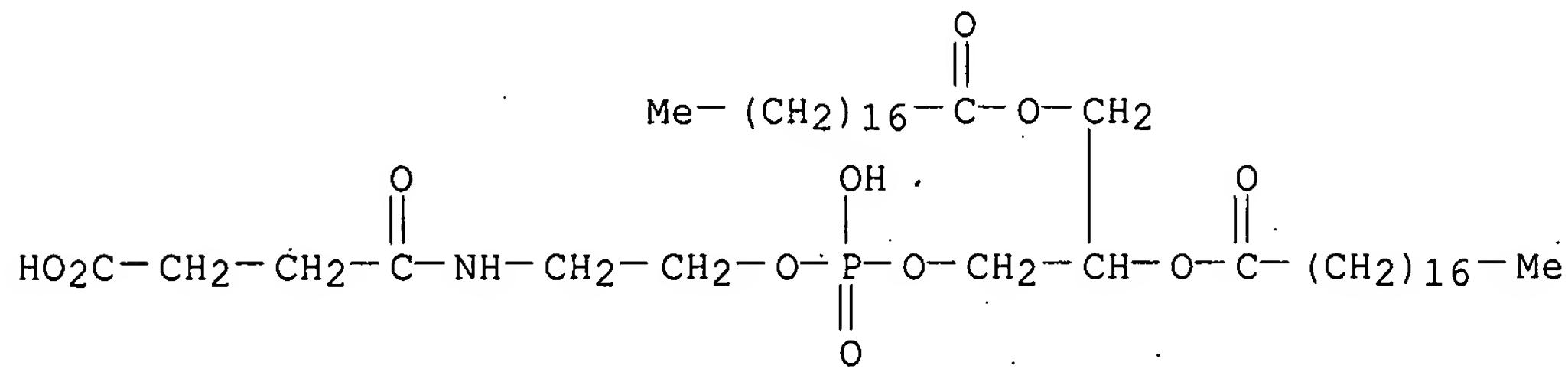
RN 766509-39-1 CAPLUS

CN Oxirane, methyl-, polymer with oxirane, mono[9-hydroxy-9-oxido-4,15-dioxo-12-[(1-oxooctadecyl)oxy]-8,10,14-trioxa-5-aza-9-phosphadotriacontanoate], methyl ether (9CI) (CA INDEX NAME)

CM 1

CRN 161693-70-5

CMF C45 H86 N O11 P



CM 2

CRN 67-56-1

CMF C H4 O

H<sub>3</sub>C-OH

CM 3

CRN 9003-11-6

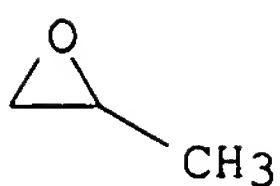
CMF (C<sub>3</sub> H<sub>6</sub> O . C<sub>2</sub> H<sub>4</sub> O)x

CCI PMS

CM 4

CRN 75-56-9

CMF C<sub>3</sub> H<sub>6</sub> O



CM 5

CRN 75-21-8

CMF C<sub>2</sub> H<sub>4</sub> O



AN 2004:681677 CAPLUS  
DN 141:212755  
TI Liposomes containing an integrin antagonist as targeting molecule  
IN Alters, Susan E.; Cleland, Jeffrey Lynn; Garzone, Pamela C.; Pease, John  
S.; Wartchow, Charles Aaron  
PA Targesome Inc., USA  
SO PCT Int. Appl., 82 pp.  
CODEN: PIXXD2

DT Patent  
LA English

FAN.CNT 1

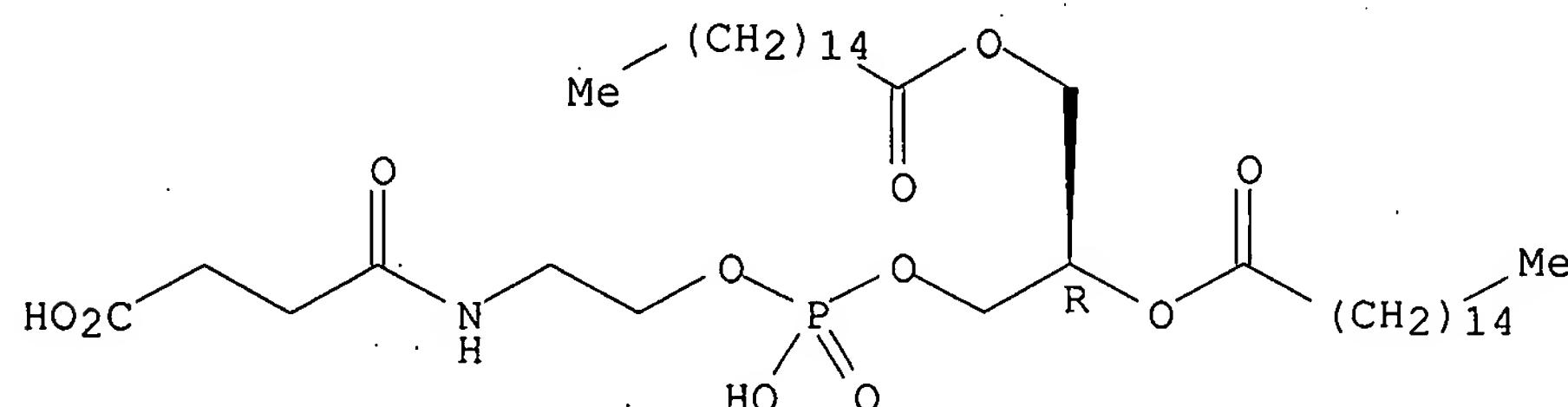
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004070009	A2	20040819	WO 2004-US2816	20040202
	WO 2004070009	A3	20050407		
		W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI		
		RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG		

PRAI US 2003-443954P P 20030131  
US 2003-458709P P 20030328  
US 2003-463581P P 20030416

AB Targeted macromols. comprising a stabilizing agent-coated liposome and more than one targeting entity, i.e., an integrin antagonist, are provided, as well as methods for their preparation and use. The stabilizing agent is selected from polymers, biopolymers, proteins, etc., e.g., dextran or modified dextran. For example, antitumor efficacy of liposomes containing an  $\alpha$ V $\beta$ 3-integrin antagonist 4-[2-(3,4,5,6-tetrahydropyrimidin-2-ylamino)ethoxy]benzoyl-2-(S)-aminoethylsulfonylamino- $\beta$ -alanine (IA, preparation given) as targeting moiety and coated with amine-modified dextran was evaluated in vivo in the U251 orthotopic glioma model in nude mice. Treatment with IA-containing dextran-coated liposomes (IA-DCL) significantly reduced tumor growth when compared to treatment with saline alone. The percentage of human tumor cells, as assessed by staining with an antibody to HLA class I, was reduced from 6.8% in control mice down to 3% following IA-DCL treatment, a reduction of approx. 50%. The IA-DCL binds to  $\alpha$ V $\beta$ 3-integrin, located on the surface of endothelial cells, blocking cell adhesion and migration and also causing apoptosis.

IT 150525-42-1  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(stabilizing agent-coated liposomes containing integrin antagonist as targeting moiety)  
RN 150525-42-1 CAPLUS  
CN 8,10,14-Trioxa-5-aza-9-phosphatricontanoic acid, 9-hydroxy-4,15-dioxo-12-[(1-oxohexadecyl)oxy]-, 9-oxide, (12R)- (CA INDEX NAME)

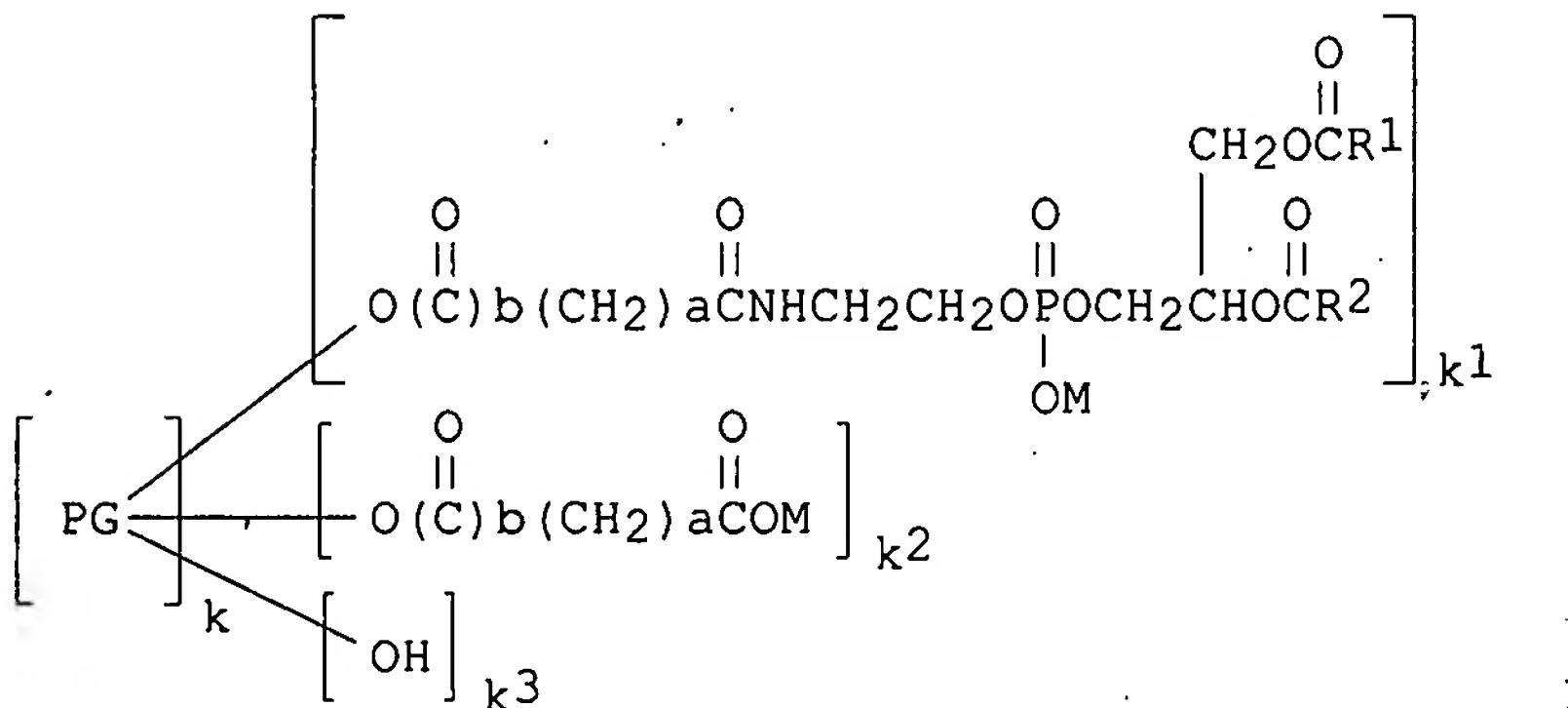
Absolute stereochemistry.



L10 ANSWER 10 OF 30 CAPLUS COPYRIGHT 2007 ACS on STN  
 AN 2004:589555 CAPLUS  
 DN 141:142211  
 TI Phospholipid derivatives used for surfactants, solubilizers, dispersants  
 in cosmetics and lipid membranes and their preparation  
 IN Kubo, Kazuhiro; Itoh, Chika; Ohhashi, Syunsuke; Yasukohchi, Tohru; Ohkawa,  
 Yusuke; Kikuchi, Hiroshi; Suzuki, Norio; Kurosawa, Miho; Yamauchi, Hitoshi  
 PA NOF Corporation, Japan; Daiichi Pharmaceutical Co., Ltd.  
 SO PCT Int. Appl., 52 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA Japanese  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004060899	A1	20040722	WO 2003-JP15969	20031212
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2513144	A1	20040722	CA 2003-2513144	20031212
	AU 2003289070	A1	20040729	AU 2003-289070	20031212
	EP 1591447	A1	20051102	EP 2003-778894	20031212
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	CN 1735624	A	20060215	CN 2003-80108368	20031212
	US 2006210618	A1	20060921	US 2005-541309	20050705
PRAI	JP 2003-330	A	20030106		
	WO 2003-JP15969	W	20031212		

GI



AB The phospholipid derivs. I ( $[PG]_k$  = residue of a polyglycerol having d.p.  $k$ ;  $k = 2-50$ ;  $R_1CO, R_2CO = C8-22$  acyl;  $a = 0-5$ ;  $b = 0-1$ ;  $M = H, \text{alkali metal, ammonium or organic ammonium}$ ; and  $k_1, k_2, k_3 = \text{nos. satisfying the relationships: } 1 \leq k_1 \leq (k + 2)/2, 0 \leq k_2, \text{ and } k_1 + k_2 + k_3 = k + 2$ ). The derivs. are highly safe for the living body and can be favorably utilized in drug delivery systems such as liposome.  
 IT 725724-27-6P 725724-29-8P 725724-33-4P

RL: BUU (Biological use, unclassified); COS (Cosmetic use); IMF (Industrial manufacture); TEM (Technical or engineered material use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of phospholipid derivs. used for surfactants, solubilizers, dispersants in cosmetics and lipid membranes)

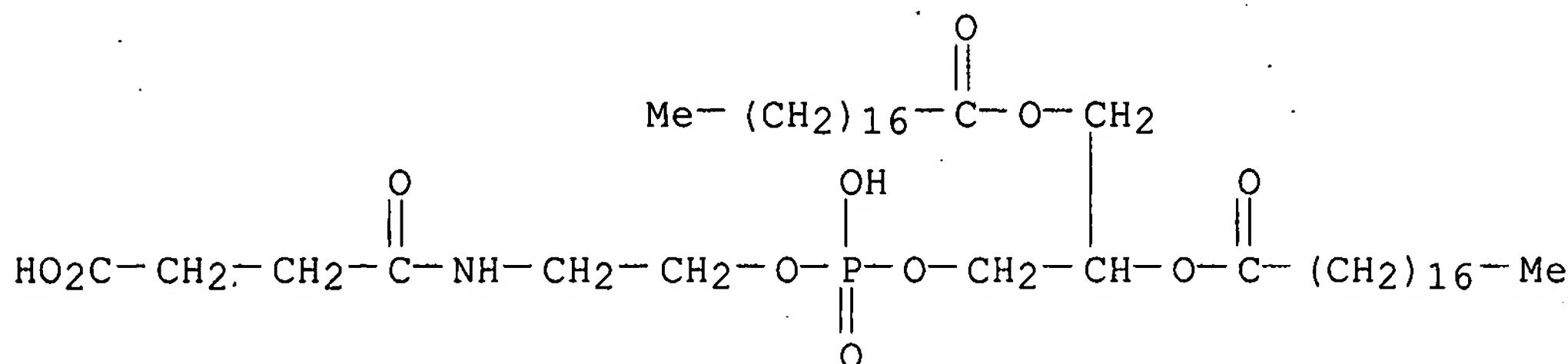
RN 725724-27-6 CAPLUS

CN 8,10,14-Trioxa-5-aza-9-phosphadotriacontanoic acid, 9-hydroxy-4,15-dioxo-12-[(1-oxooctadecyl)oxy]-, 9-oxide, ester with octaglycerol (9CI) (CA INDEX NAME)

CM 1

CRN 161693-70-5

CMF C45 H86 N O11 P



CM 2

CRN 70103-30-9

CMF C24 H50 O17

CCI IDS, MAN

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

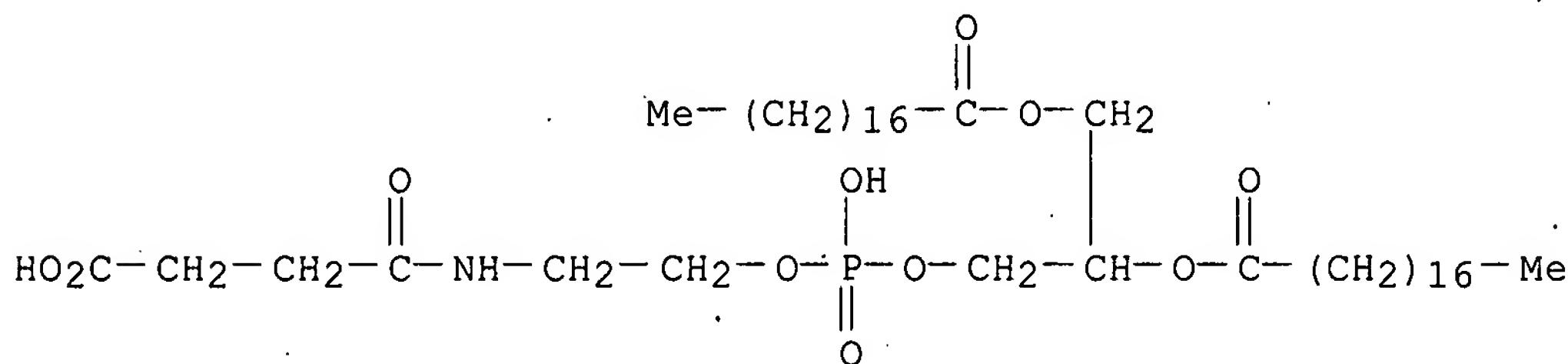
RN 725724-29-8 CAPLUS

CN 1,2,3-Propanetriol, homopolymer, mono[9-hydroxy-9-oxido-4,15-dioxo-12-[(1-oxooctadecyl)oxy]-8,10,14-trioxa-5-aza-9-phosphadotriacontanoate] (9CI) (CA INDEX NAME)

CM 1

CRN 161693-70-5

CMF C45 H86 N O11 P



CM 2

CRN 25618-55-7

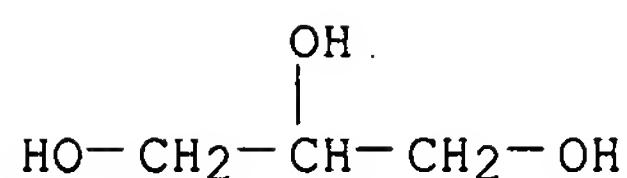
CMF (C<sub>3</sub> H<sub>8</sub> O<sub>3</sub>)<sub>x</sub>

CCI PMS

CM 3

CRN 56-81-5

CMF C3 H8 O3



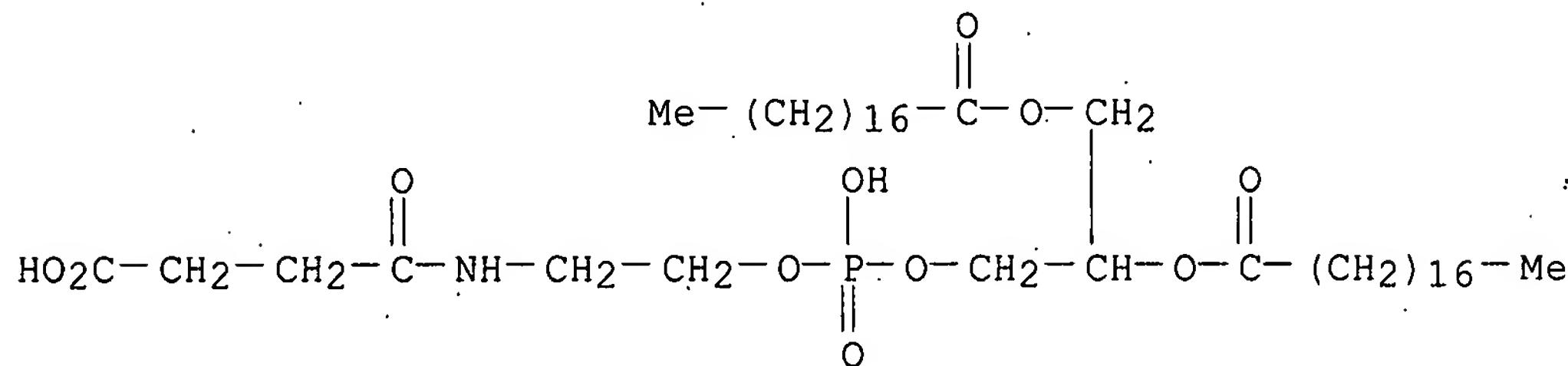
RN 725724-33-4 CAPLUS

CN 8,10,14-Trioxa-5-aza-9-phosphadтриаcontanoic acid, 9-hydroxy-4,15-dioxo-12-[(1-oxooctadecyl)oxy]-, 9-oxide, ester with hexaglycerol (9CI) (CA INDEX NAME)

CM 1

CRN 161693-70-5

CMF C45 H86 N O11 P



CM 2

CRN 36675-34-0

CMF C18 H38 O13

CCI IDS, MAN

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

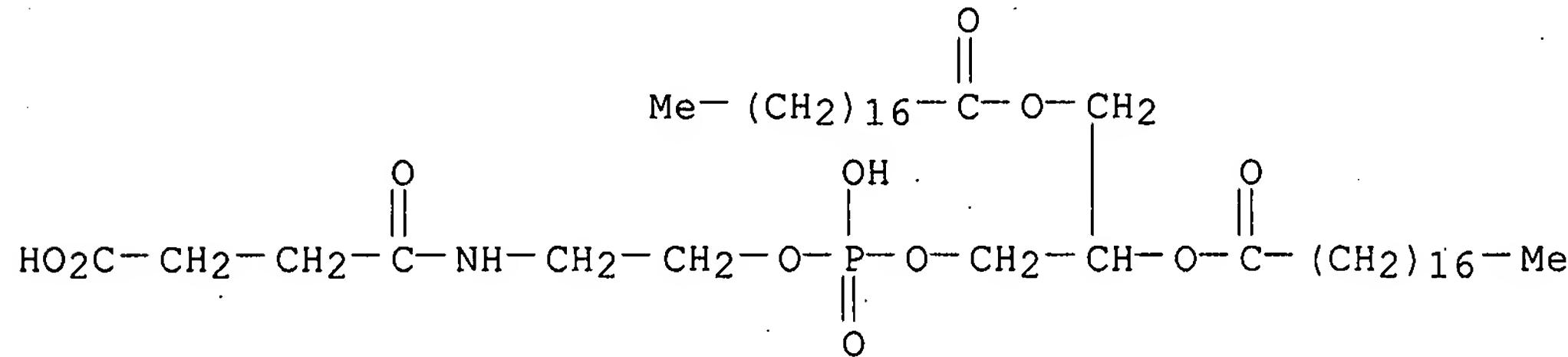
IT 161693-70-5P

RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)

(preparation of phospholipid derivs. used for surfactants, solubilizers, dispersants in cosmetics and lipid membranes)

RN 161693-70-5 CAPLUS

CN 8,10,14-Trioxa-5-aza-9-phosphadтриаcontanoic acid, 9-hydroxy-4,15-dioxo-12-[(1-oxooctadecyl)oxy]-, 9-oxide (9CI) (CA INDEX NAME)



AN 2003:796716 CAPLUS  
DN 139:296564  
TI Phospholipid derivatives for cosmetic and pharmaceutical uses  
IN Itoh, Chika; Kubo, Kazuhiro; Ohhashi, Syunsuke; Yasukohchi, Tohru;  
Kikuchi, Hiroshi; Suzuki, Norio; Kurosawa, Miho; Yamauchi, Hitoshi  
PA NOF Corporation, Japan; Daiichi Pharmaceutical Co., Ltd.  
SO PCT Int. Appl., 47 pp.  
CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003082882	A1	20031009	WO 2003-JP3966	20030328
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2003220917	A1	20031013	AU 2003-220917	20030328
	EP 1498420	A1	20050119	EP 2003-715589	20030328
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	US 2005220856	A1	20051006	US 2005-508704	20050525

PRAI JP 2002-93694 A 20020329  
WO 2003-JP3966 W 20030328

AB Disclosed is a phospholipid derivative which is highly safe for the living body and is suitable for use in solubilizing or dispersing a physiol. active substance, etc. or in the field of drug delivery systems, e.g., a liposome, or cosmetics. The phospholipids comprise polyalkylene oxide groups. For example, polyoxyethylene pentaerythritol ether glutaryl-mono(distearoylphosphatidylethanolamine succinate) was prepared and used as a solubilizer in formulating lotions.

IT 609816-64-0P, Polyoxyethylene hexaglycerol ether-mono(distearoylphosphatidylethanolamine succinate) 609816-65-1P, Polyoxyethylene hexaglycerol ether glutaryl-mono(distearoylphosphatidylethanolamine succinate) 609844-38-4P  
RL: COS (Cosmetic use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of phospholipid derivs. for cosmetic and pharmaceutical uses)

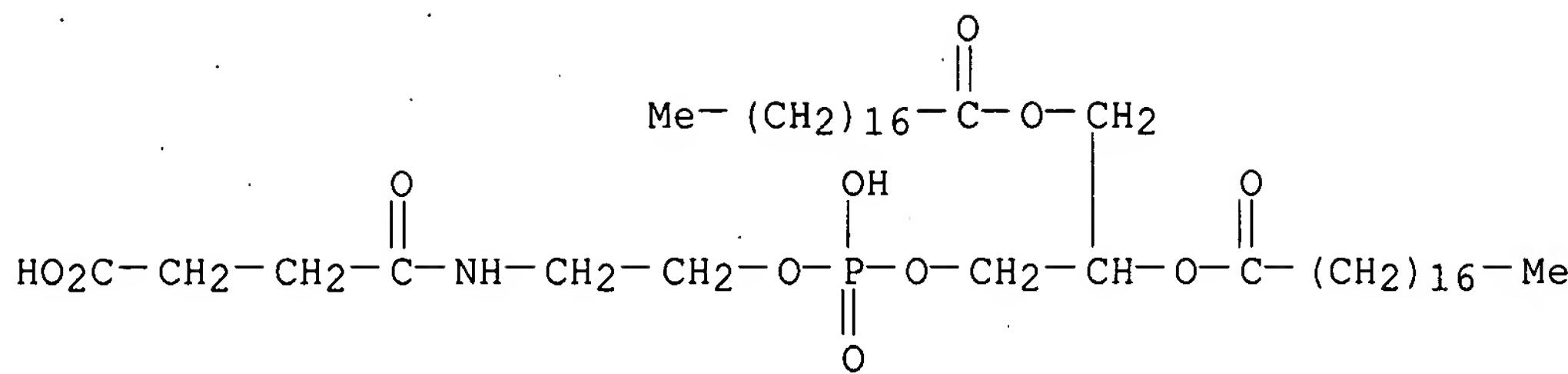
RN 609816-64-0 CAPLUS

CN Poly(oxy-1,2-ethanediyl),  $\alpha$ -hydro- $\omega$ -hydroxy-, ether with hexaglycerol, 9-hydroxy-9-oxido-4,15-dioxo-12-[(1-oxooctadecyl)oxy]-8,10,14-trioxa-5-aza-9-phosphadotriacontanoate (9CI) (CA INDEX NAME)

CM 1

CRN 161693-70-5

CMF C45 H86 N O11 P



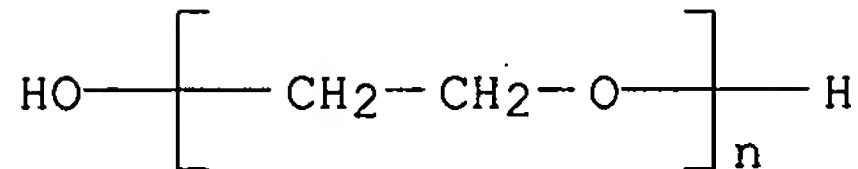
CM 2

CRN 36675-34-0  
 CMF C18 H38 O13  
 CCI IDS, MAN

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

CM 3

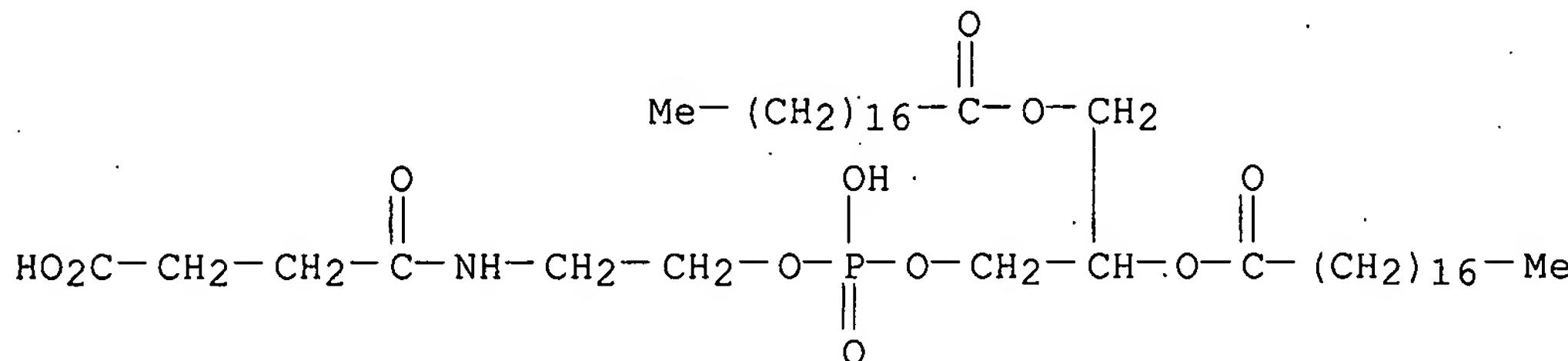
CRN 25322-68-3  
 CMF (C<sub>2</sub> H<sub>4</sub> O)<sub>n</sub> H<sub>2</sub> O  
 CCI PMS



RN 609816-65-1 CAPLUS  
 CN Poly(oxy-1,2-ethanediyl),  $\alpha$ -hydro- $\omega$ -hydroxy-, ether with hexaglycerol, 9-hydroxy-9-oxido-4,15-dioxo-12-[(1-oxooctadecyl)oxy]-8,10,14-trioxa-5-aza-9-phosphadotriacontanoate pentanedioate (9CI) (CA INDEX NAME)

CM 1

CRN 161693-70-5  
 CMF C45 H86 N O11 P



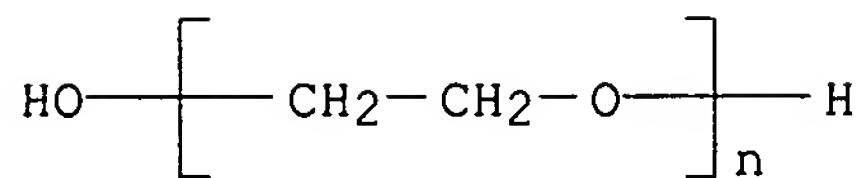
CM 2

CRN 36675-34-0  
 CMF C18 H38 O13  
 CCI IDS, MAN

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

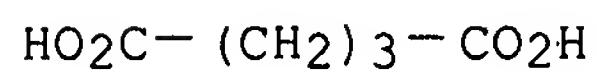
CM 3

CRN 25322-68-3  
CMF (C<sub>2</sub> H<sub>4</sub> O)<sub>n</sub> H<sub>2</sub>O  
CCI PMS



CM 4

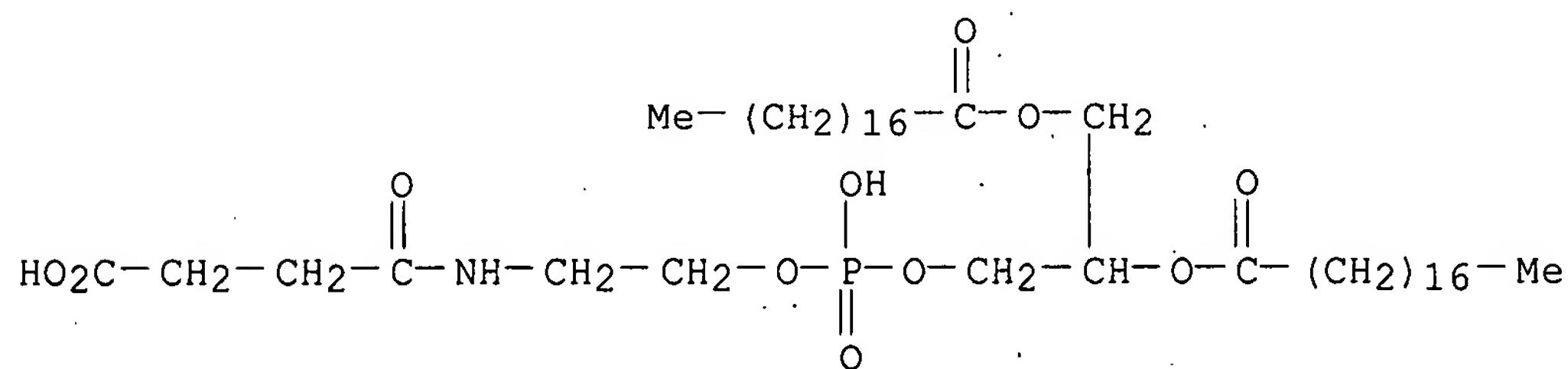
CRN 110-94-1  
CMF C<sub>5</sub> H<sub>8</sub> O<sub>4</sub>



RN 609844-38-4 CAPLUS  
CN Poly(oxy-1,2-ethanediyl),  $\alpha,\alpha',\alpha''$ -1,2,3-propanetriyltris[ $\omega$ -hydroxy-, mono(9-hydroxy-9-oxido-4,15-dioxo-12-[(1-oxooctadecyl)oxy]-8,10,14-trioxa-5-aza-9-phosphadotriacontanoate) (9CI) (CA INDEX NAME)

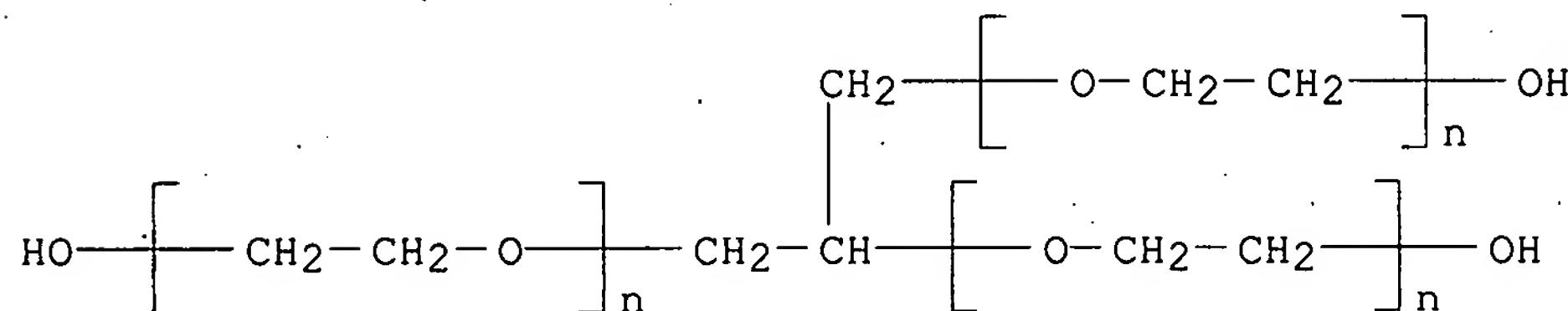
CM 1

CRN 161693-70-5  
CMF C<sub>45</sub> H<sub>86</sub> N O<sub>11</sub> P



CM 2

CRN 31694-55-0  
CMF (C<sub>2</sub> H<sub>4</sub> O)<sub>n</sub> (C<sub>2</sub> H<sub>4</sub> O)<sub>n</sub> (C<sub>2</sub> H<sub>4</sub> O)<sub>n</sub> C<sub>3</sub> H<sub>8</sub> O<sub>3</sub>  
CCI PMS



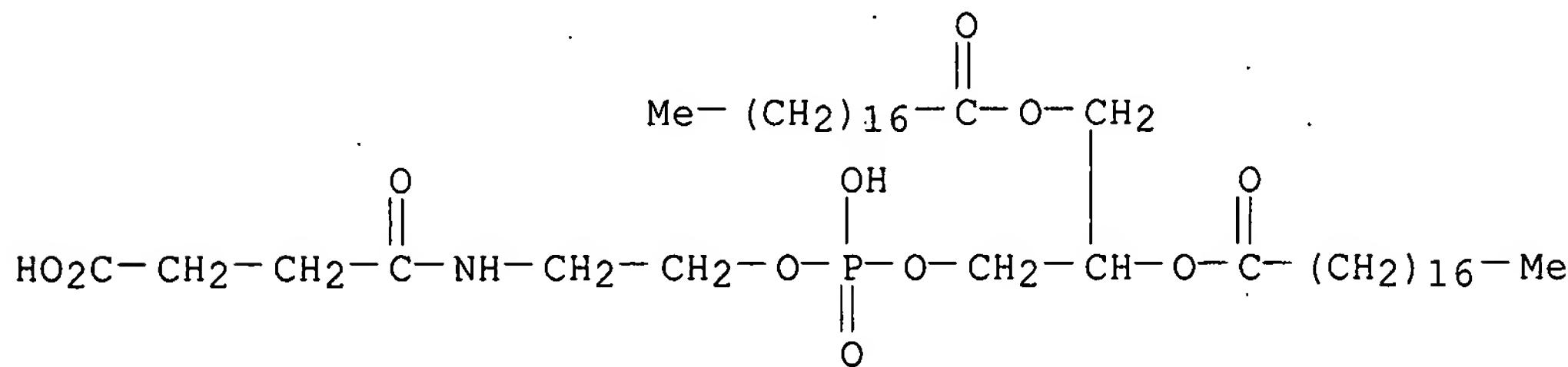
IT 161693-70-5P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)

(preparation of phospholipid derivs. for cosmetic and pharmaceutical uses)

RN 161693-70-5 CAPLUS

CN 8,10,14-Trioxa-5-aza-9-phosphadotriacontanoic acid, 9-hydroxy-4,15-dioxo-  
12-[(1-oxooctadecyl)oxy]-, 9-oxide (9CI) (CA INDEX NAME)



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 12 OF 30 CAPLUS COPYRIGHT 2007 ACS on STN  
AN 2003:532140 CAPLUS  
DN 139:106450  
TI Targeted multivalent macromolecules  
IN Wartchow, Charles Aaron; Dechene, Neal Edward; Pease, John S.; Shen, Zhimin; Trulson, Julie; Bednarski, Mark David; Danthi, S. Narasimhan; Zhang, Michael; Choi, Hoyul Steven  
PA Targesome, Inc., USA  
SO U.S. Pat. Appl. Publ., 71 pp., Cont.-in-part of U.S. Ser. No. 976,254.  
CODEN: USXXCO  
DT Patent  
LA English

FAN.CNT 9

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003129223	A1	20030710	US 2002-158777	20020530
	US 2002071843	A1	20020613	US 2001-976254	20011011
	ZA 2003009924	A	20050622	ZA 2003-9924	20031222
	US 2006188560	A1	20060824	US 2006-396743	20060403
PRAI	US 2000-239684P	P	20001011		
	US 2001-294309P	P	20010530		
	US 2001-309104P	P	20010731		
	US 2001-312435P	P	20010815		
	US 2001-976254	A2	20011011		
	US 2001-345891P	P	20011029		
	US 2002-158761	A3	20020530		

AB Targeted therapeutic agents, comprising a linking carrier, a therapeutic entity associated with the linking carrier, and at least one targeting entity are provided, as well as methods for their preparation and use. A targeted therapeutic agent is selected from matrix metalloprotease inhibitors, analgesics, aggrecanase inhibitors, alkylating agents, topoisomerase inhibitors, estrogens, androgens, interferons, intercalating agents, kinase modulators, etc. The linking carrier comprises a phosphatidylcholine and is selected from liposomes and a polymerized vesicle. A targeting entity targets a lipid construct to a target selected from a cell surface target, an intracellular target, and an extracellular matrix component. The targeting entity has, e.g., a vascular or tumor cell target selected from chemokine receptors, matrix metalloproteases, integrins, or prostate-specific membrane antigens. For example, integrin-targeted 90Y-labeled peptidomimetic vesicle complexes (IA-NP-Y90) at 5  $\mu$ Ci/g reduced tumor growth in a melanoma mouse model with average normalized tumor volume less than half the volume in the buffer-treated animals. In addition, the average tumor volume quadrupling time (TVQT) for tumor

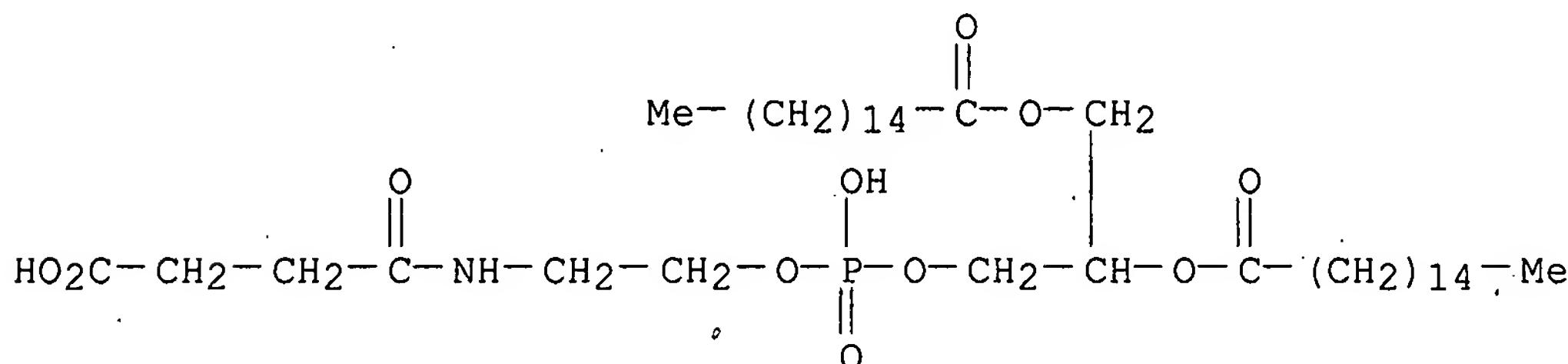
treated with IA-NP-Y90 was 15.0 days compared to 6.4 days for tumors treated with buffer.

IT 88848-80-0

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (preparation of targeted multivalent macromols. for therapy, imaging and diagnosis of cancer)

RN 88848-80-0 CAPLUS

CN 8,10,14-Trioxa-5-aza-9-phosphatricontanoic acid, 9-hydroxy-4,15-dioxo-12-[(1-oxohexadecyl)oxy]-, 9-oxide (9CI) (CA INDEX NAME)



L10 ANSWER 13 OF 30 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2002:778699 CAPLUS

DN 137:299916

TI Peptide-containing compounds for targeting cells expressing NP-1 receptor

IN Von Wronski, Mathew A.; Marinelli, Edmund R.; Nunn, Adrian D.; Pillai, Radhakrishna; Ramalingam, Kondareddiar; Tweedle, Michael F.; Linder, Karen; Nanjappan, Palaniappa; Raju, Natarajan

PA USA

SO U.S. Pat. Appl. Publ., 85 pp., Cont.-in-part of U.S. Ser. No. 585,364.  
CODEN: USXXCO

DT Patent

LA English

FAN.CNT 3

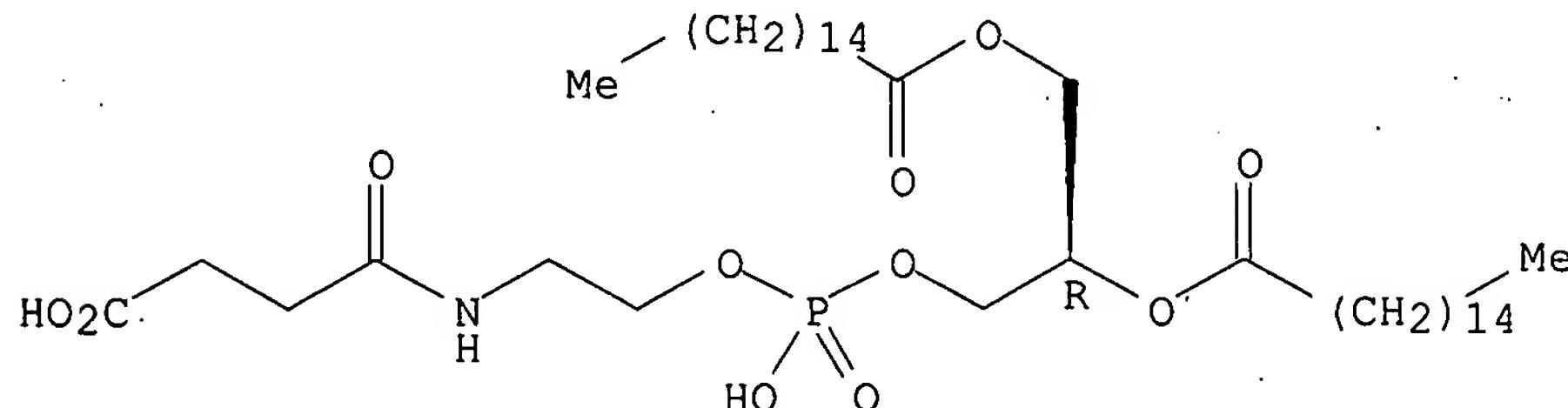
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002147136	A1	20021010	US 2001-871974	20010604
	US 7109167	B2	20060919		
	US 2006153775	A1	20060713	US 2006-342050	20060127
	US 2006258566	A1	20061116	US 2006-381884	20060505
	US 2006263303	A1	20061123	US 2006-381908	20060505
PRAI	US 2000-585364	A2	20000602		
	US 2001-871974	A2	20010604		

OS MARPAT 137:299916

AB The present invention provides compds. for targeting endothelial cells, tumor cells or other cells that express the neuropilin-1 (NP-1) receptor, compns. containing the same and methods for their use. The compds. are of the formula A-L-B (A = a monomer, multimer or polymer of TKPPR or analog which specifically binds to NP-1 or cells expressing NP-1 with avidity equal or greater than TKPPR; L = a lipid or a non-lipid (e.g., polymer) linker; B = a substrate). Addnl., the present invention includes diagnostic, therapeutic and radiotherapeutic compns. useful for visualization, therapy or radiotherapy. For example, DPPE-glutaroyl-Gly-Thr-Lys-Pro-Pro-Arg-OH (DPPE-Glu-GTKPPR) was prepared and formulated into gas-filled microbubble compns. for ultrasonic echog. The bubbles bind to human aortic endothelial cells (HAEC) under flow. The number of bubbles bound may increase with time for several minutes at a given flow rate, up to a flow rate producing 1.53 dynes/cm<sup>2</sup>, while bubbles without the targeting moiety (DPPE-Glu-GTKPPR) may not bind. However, once bound under a lesser flow rate (e.g., 1.53 dynes/cm<sup>2</sup>), the shear stress on bubbles containing DPPE-Glu-GTKPPR may be increased to 6.1 dynes/cm<sup>2</sup> without dislodging many of the bound bubbles.

IT 150525-42-1P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation of peptide-containing compds. and compns. for targeting cells  
 expressing neuropilin-1 receptor for diagnosis, imaging, and therapy)  
 RN 150525-42-1 CAPLUS  
 CN 8,10,14-Trioxa-5-aza-9-phosphatricontanoic acid, 9-hydroxy-4,15-dioxo-12-  
 [(1-oxohexadecyl)oxy]-, 9-oxide, (12R)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 14 OF 30 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2002:353313 CAPLUS

DN 136:355484

TI Novel targeted compositions for diagnostic and therapeutic use

IN Unger, Evan C.; Matsunaga, Terry O.; Schumann, Patricia A.

PA ImaRx Therapeutics, Inc., USA

SO PCT Int. Appl., 206 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002036161	A2	20020510	WO 2001-US32308	20011017
	WO 2002036161	A3	20030925		
	W: AU, CA, JP				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,				
	PT, SE, TR				
	CA 2428606	A1	20020510	CA 2001-2428606	20011017
	AU 200213285	A	20020515	AU 2002-13285	20011017
	EP 1365805	A2	20031203	EP 2001-981655	20011017
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				
	IE, FI, CY, TR				
	JP 2005500245	T	20050106	JP 2002-538970	20011017
PRAI	US 2000-699679	A	20001030		
	WO 2001-US32308	W	20011017		

OS MARPAT 136:355484

AB Novel targeted compns. which may be used for diagnostic and therapeutic use may comprise lipid, protein or polymer gas-filled vesicles which further comprise novel compds. of formula L-P-T, where L is a hydrophobic compound, P is a hydrophilic polymer, and T is a targeting ligand which targets tissues, cells or receptors, including myocardial cells, endothelial cells, epithelial cells, tumor cells and the glycoprotein GPIIbIIIa receptor. Compds. R1R2N-R3-CH(NR4R5)-R6-X1-P-R7-X2-T [X1, X2 is a direct bond or a linking atom or group; R1, R4 = C7-23 acyl; R2, R5 = H or lower alkyl; R3, R6, R7 = a direct bond or C1-10 alkylene; same P and T] are claimed. The compns. can be used in conjunction with diagnostic imaging, such as ultrasound, as well as therapeutic applications, such as therapeutic ultrasound. Examples include the preparation of

N,N'-bis(hexadecylaminocarbonylmethyl)-N,N'-bis[ $\beta$ -  
(trimethylammonio)ethylaminocarbonylmethyl]-N,N'-dimethylethylenediamine  
tetraiodide and N-(1,2-dipalmitoyl-sn-glycero-3-succinyl)-PEG-protein A  
conjugate. Videodensitometric anal. of targeted vesicles-ultrasound  
backscatter quantitation is shown in a table.

IT

150525-42-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)

(targeted compns. for diagnostic and therapeutic use)

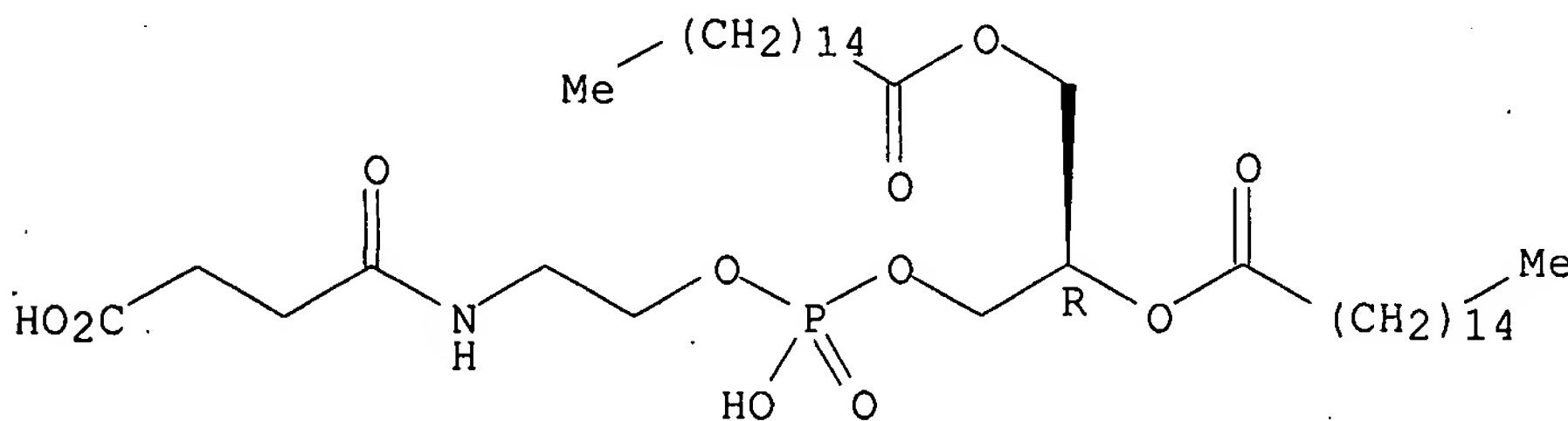
RN

150525-42-1 CAPLUS

CN

8,10,14-Trioxa-5-aza-9-phosphatriacontanoic acid, 9-hydroxy-4,15-dioxo-12-  
[(1-oxohexadecyl)oxy]-, 9-oxide, (12R)- (CA INDEX NAME)

Absolute stereochemistry.



L10 ANSWER 15 OF 30 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2001:704741 CAPLUS

DN 135:273165

TI Method for preparation of phosphatidylethanolamine derivatives by  
amidation of diacylphosphatidylethanolamine with dicarboxylic anhydride

IN Maekawa, Naoya; Oda, Hiroshi; Matsuyoshi, Shigeru

PA NOF Corporation, Japan

SO Jpn. Kokai Tokkyo Koho, 5 pp.

CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 2001261688	A	20010926	JP 2000-79696	20000322
PRAI	JP 2000-79696		20000322		

OS CASREACT 135:273165; MARPAT 135:273165

AB The title compds. represented by formula R<sub>1</sub>OCH<sub>2</sub>CH(OR<sub>2</sub>)CH<sub>2</sub>OP(O)(OM<sub>1</sub>)OCH<sub>2</sub>CH<sub>2</sub>  
NHCO(CH<sub>2</sub>)<sub>n</sub>CO<sub>2</sub>M<sub>2</sub> (R<sub>1</sub>, R<sub>2</sub> = aliphatic acyl; M<sub>1</sub>, M<sub>2</sub> = H, alkali or alkaline earth  
metal, ammonium; n = an integer of 1-14) are prepared by reaction of  
diacylphosphatidylethanolamine and dicarboxylic anhydride using an organic  
solvent not having an active hydrogen, mixing the reaction mixture with a  
buffer solution (pH 3.5-7.5), separating the organic phase, and removing the  
organic

solvent from the organic phase. This process gives N-acyl-  
diacylphosphatidylethanolamines (glycerophospholipids) of high purity  
( $\geq$ 97%) in high yields ( $\geq$ 90%) and is industrially  
advantageous since it does not require complicated procedures such as  
silica gel chromatog. Thus, 1.0 g dioleoylphosphatidylethanolamine  
( $\geq$ 99.5% purity) and 1.66 g Et<sub>3</sub>N were dissolved in 200 mL CHCl<sub>3</sub>,  
treated with 2.2. g glutaric anhydride, stirred at 4° for 1 h, and  
mixed with 0.5 M AcONa/AcOH buffer (pH 6). The reaction mixture was  
transferred to a separatory funnel and left to stand for 1 h and the  
bottom layer was separated. The bottom layer was treated again with AcONa/AcOH  
buffer (pH 6) as described above and the organic layer was separated. The  
organic solvent was distilled off and the residue was dispersed in water for

injection and freeze-dried to give 11.6 g 1,2-dioleoyl-sn-glycero-3-phospho-O-(N-glutaryl)ethanolamine sodium salt (99.7% purity) in 97.8% yield.

IT 362685-26-5P

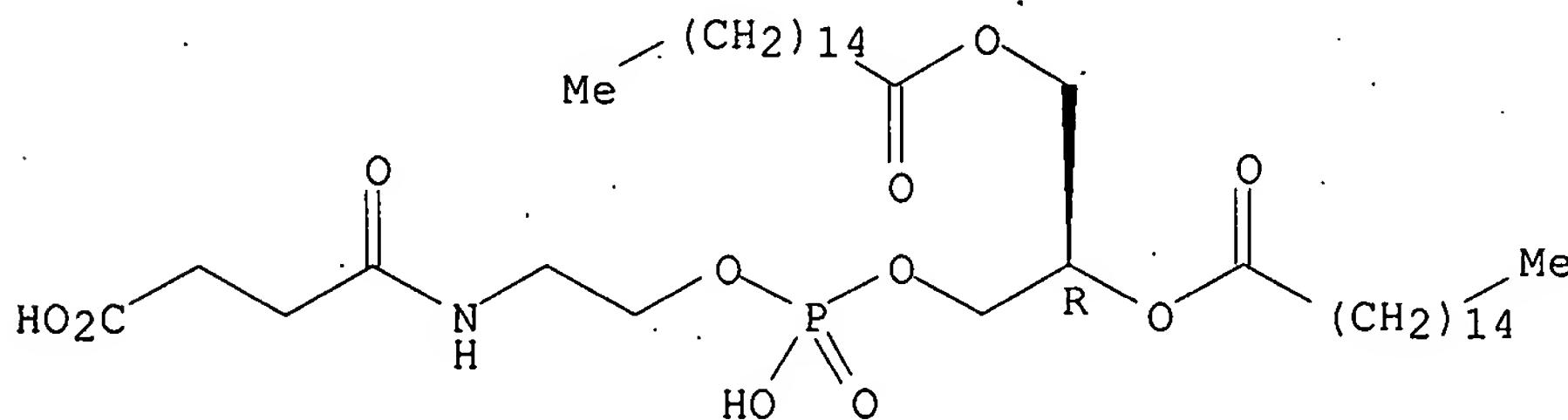
RL: BUU (Biological use, unclassified); IMF (Industrial manufacture); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)

(method for preparation of phosphatidylethanolamine derivs. as glycerophospholipids by amidation of diacylphosphatidylethanolamine with dicarboxylic anhydride)

RN 362685-26-5 CAPLUS

CN 8,10,14-Trioxa-5-aza-9-phosphatriacontanoic acid, 9-hydroxy-4,15-dioxo-12-[(1-oxohexadecyl)oxy]-, 9-oxide, disodium salt, (12R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●2 Na

IT 150525-42-1P 248253-94-3P

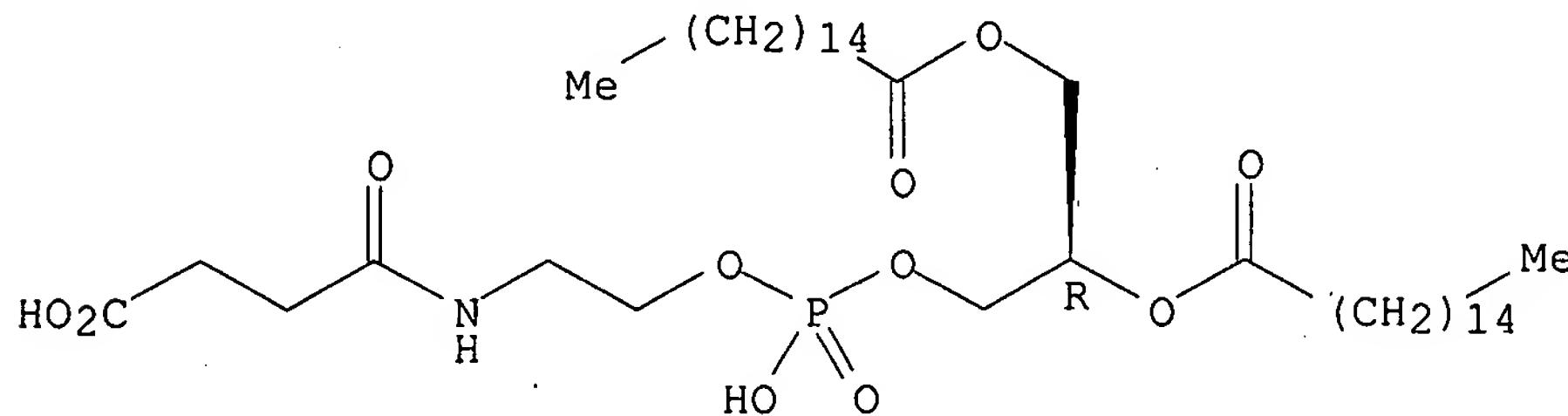
RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)

(method for preparation of phosphatidylethanolamine derivs. as glycerophospholipids by amidation of diacylphosphatidylethanolamine with dicarboxylic anhydride)

RN 150525-42-1 CAPLUS

CN 8,10,14-Trioxa-5-aza-9-phosphatriacontanoic acid, 9-hydroxy-4,15-dioxo-12-[(1-oxohexadecyl)oxy]-, 9-oxide, (12R)- (CA INDEX NAME)

Absolute stereochemistry.



RN 248253-94-3 CAPLUS

CN 8,10,14-Trioxa-5-aza-9-phosphadotriacontanoic acid, 9-hydroxy-4,15-dioxo-12-[(1-oxooctadecyl)oxy]-, 9-oxide, (12R)- (CA INDEX NAME)

Absolute stereochemistry.



microbubbles encapsulated with distearoylphosphatidylserine doped with Mal-PEG2000-distearoylphosphatidylethanolamine (DSPE) was prepared and reacted with thiolated anti-CD34 antibodies to make a reagent useful for separating CD34-pos. cells.

IT 248253-94-3

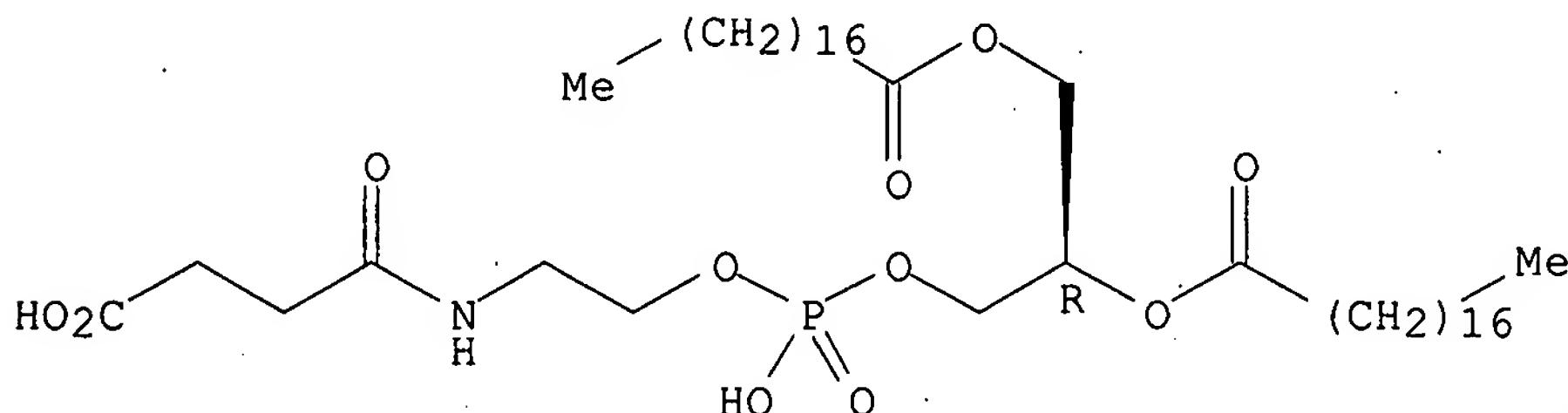
RL: RCT (Reactant); RACT (Reactant or reagent)

(targetable encapsulated gas microbubbles for separation of target material from liquid samples and separation apparatus)

RN 248253-94-3 CAPLUS

CN 8,10,14-Trioxa-5-aza-9-phosphadotriacontanoic acid, 9-hydroxy-4,15-dioxo-12-[(1-oxooctadecyl)oxy]-, 9-oxide, (12R)- (CA INDEX NAME)

Absolute stereochemistry.



L10 ANSWER 17 OF 30 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1999:220014 CAPLUS

DN 130:249137

TI Novel targeted ultrasound imaging contrast agents for diagnostic and therapeutic use

IN Unger, Evan C.; Fritz, Thomas A.; Gertz, Edward W.

PA ImarRx Pharmaceutical Corp., USA

SO PCT Int. Appl., 223 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 8

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9913919	A1	19990325	WO 1998-US18858	19980909
	W: AU, CA				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 6139819	A	20001031	US 1997-932273	19970917
	AU 9893830	A	19990405	AU 1998-93830	19980909
	EP 959908	A1	19991201	EP 1998-946919	19980909
	R: DE, FR, GB, IT				
PRAI	US 1997-932273	A	19970917		
	US 1995-497684	B2	19950607		
	US 1996-640464	B2	19960501		
	US 1996-660032	B2	19960606		
	US 1996-666129	A2	19960619		
	WO 1998-US18858	W	19980909		

AB This invention describes novel contrast agents which may be used for diagnostic and therapeutic use. The compns. may comprise a lipid, a protein, polymer and/or surfactant, and a gas, in combination with a targeting ligand. In preferred embodiments, the targeting ligand targets coagula, including emboli and/or thrombi, particularly in patients suffering from an arrhythmic disorder. The contrast media can be used in conjunction with diagnostic imaging, such as ultrasound, as well as therapeutic applications, such as therapeutic ultrasound.

IT 150525-42-1

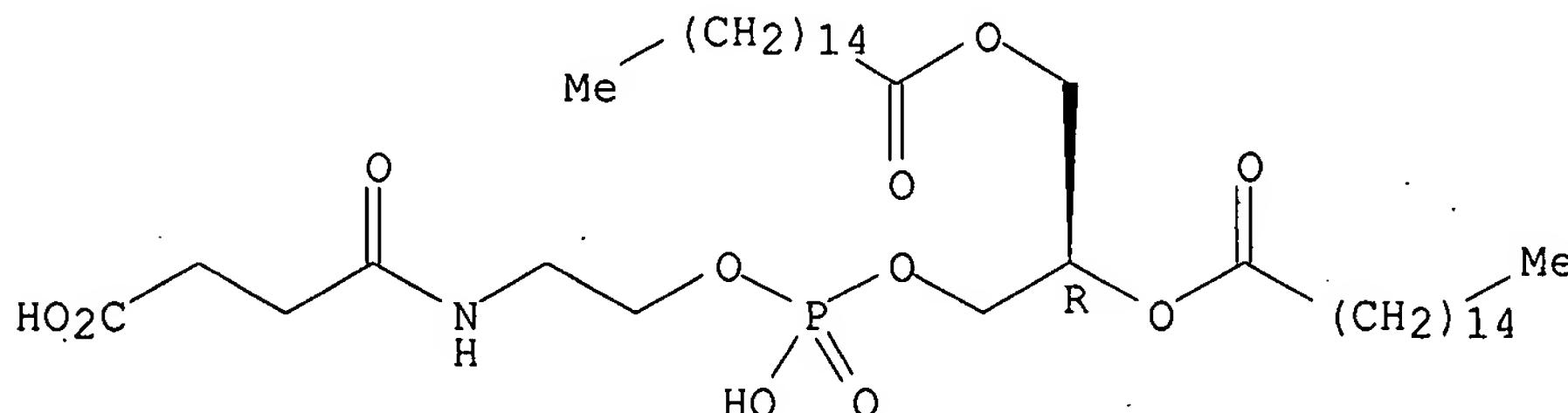
RL: RCT (Reactant); RACT (Reactant or reagent)

(novel targeted ultrasound imaging contrast agents for diagnostic and therapeutic use)

RN 150525-42-1 CAPLUS

CN 8,10,14-Trioxa-5-aza-9-phosphatricacontanoic acid, 9-hydroxy-4,15-dioxo-12-[(1-oxohexadecyl)oxy]-, 9-oxide, (12R)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 18 OF 30 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1997:601246 CAPLUS

DN 127:298616

TI Enhancement of the in vivo circulation lifetime of L- $\alpha$ -distearoylphosphatidylcholine liposomes: importance of liposomal aggregation versus complement opsonization

AU Ahl, Patrick L.; Bhatia, Suresh K.; Meers, Paul; Roberts, Patricia; Stevens, Rachel; Dause, Richard; Perkins, Walter R.; Janoff, Andrew S.

CS The Liposome Company, Inc., Princeton Forrestal Center, One Research Way, Princeton, NJ, 08540-6619, USA

SO Biochimica et Biophysica Acta, Biomembranes (1997), 1329(2), 370-382  
CODEN: BBBMBS; ISSN: 0005-2736

PB Elsevier B.V.

DT Journal

LA English

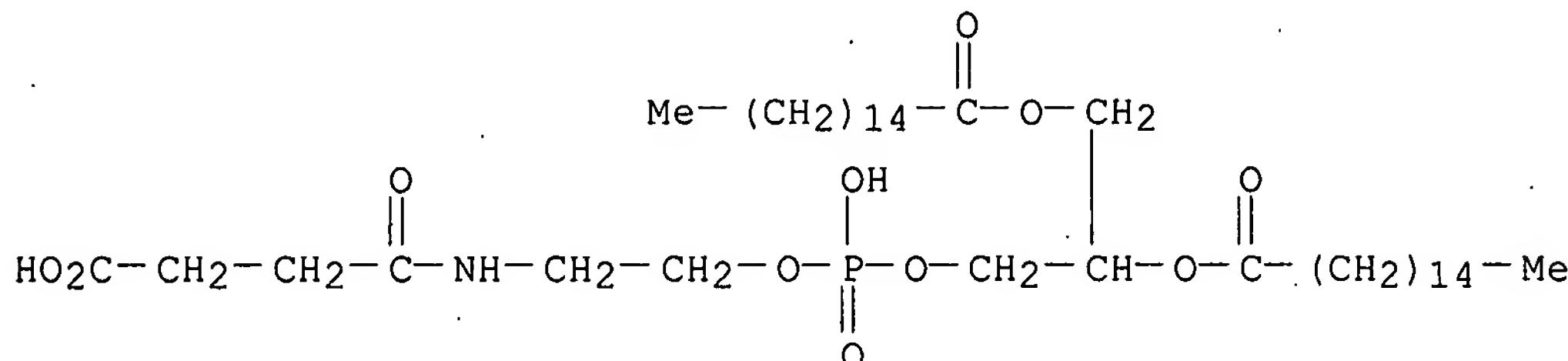
AB Incorporation of N-( $\omega$ -carboxy)acylamido-phosphatidylethanolamines (-PEs) into large unilamellar vesicles (LUVs) of L- $\alpha$ -distearoylphosphatidylcholine (DSPC) was found to dramatically increase the in vivo liposomal circulation lifetime in rats, reaching a maximal effect at 10 mol.% of the total phospholipid. Neither pure DSPC liposomes nor those with the longest circulating derivative, N-glutaryl-dipalmitoylphosphatidylethanolamine (-DPPE), were found to significantly bind complement from serum. Therefore, the relatively short circulation time of pure DSPC liposomes did not appear to be related to greater complement opsonization leading to uptake by the reticuloendothelial system. However, N-( $\omega$ -carboxy)acylamido-PEs were particularly efficient inhibitors of a limited aggregation detected for pure DSPC liposomes. The aggregation tendency of DSPC liposomes incorporating various structural analogs of N-glutaryl-DPPE correlated inversely with the circulation lifetimes. Therefore, it is concluded that such PE derivs. enhance the circulation time by preventing liposomal aggregation and avoiding a poorly understood mechanism of clearance that is dependent on size but is independent of complement opsonization. At high concns. of N-glutaryl-DPPE (above 10 mol.%), the liposomes exhibited strong complement opsonization and were cleared from circulation rapidly, as were other highly neg. charged liposomes. These data demonstrate that both the lack of opsonization and the lack of a tendency to aggregate are required for long circulation. Liposomal disaggregation via N-( $\omega$ -carboxy)acylamido-PEs yields a new class of large unilamellar DSPC liposomes with circulation lifetimes that are comparable to those of sterically stabilized liposomes.

IT 88848-80-0P

RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)  
(liposomal aggregation vs. complement opsonization in enhancement of circulation lifetime of L- $\alpha$ -distearylphosphatidylcholine liposomes)

RN 88848-80-0 CAPLUS

CN 8,10,14-Trioxa-5-aza-9-phosphatriacontanoic acid, 9-hydroxy-4,15-dioxo-12-[(1-oxohexadecyl)oxy]-, 9-oxide (9CI) (CA INDEX NAME)



RE.CNT 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 19 OF 30 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1997:594622 CAPLUS

DN 127:253188

TI Phospholipid-ligand complexes for enhancing liposomal delivery system

IN Thompson, David H.; Low, Philip S.; Rui, Yuanjin; Wang, Susan

PA Purdue Research Foundation, USA; Thompson, David H.; Low, Philip S.; Rui, Yuanjin; Wang, Susan

SO PCT Int. Appl., 40 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

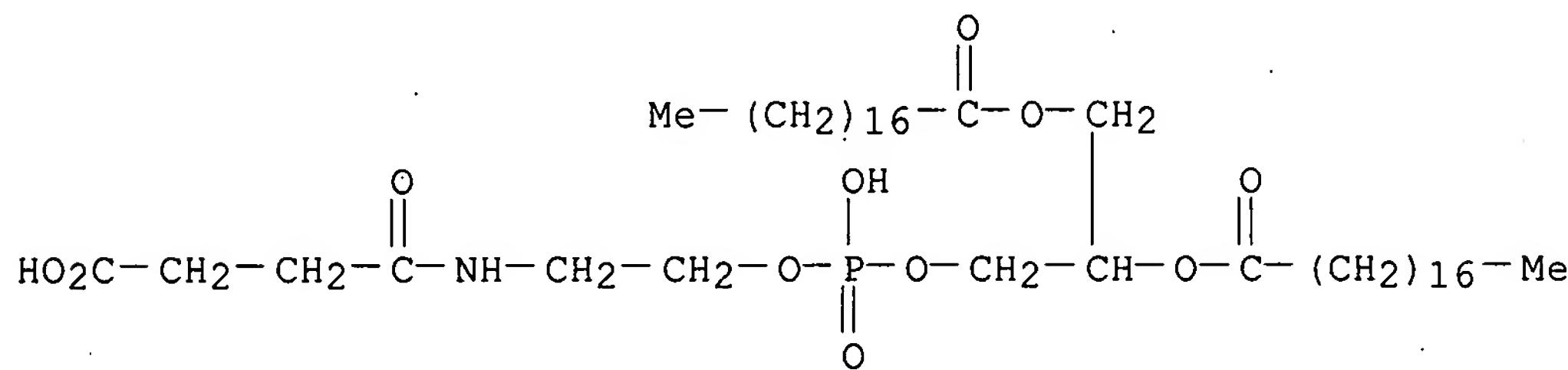
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9731624	A1	19970904	WO 1997-US3077	19970226
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9723169	A	19970916	AU 1997-23169	19970226
PRAI	US 1996-12353P	P	19960227		
	WO 1997-US3077	W	19970226		
OS	MARPAT 127:253188				
AB	An improved liposome and method for delivering an exogenous mol. to the cytoplasm of a cell is described. The liposomal membrane comprises triggerable lipids and lipids complexed to a ligand, wherein the ligand is capable of interacting with cellular membrane to enhance the uptake of the ligand and attached liposome. Dipalasmethylcholine-13.6 mg was dissolved in 0.5 mL CHCl <sub>3</sub> and 15 $\mu$ L folate-PEG-distearylphosphatidylethanolamine conjugate was added. The mixture was evaporated with a stream of dry N <sub>2</sub> , then by lyophilization to give a thin film, which was hydrated with 1 mL of propidium iodide solution to disperse the lipid as multilamellar liposomes (MLV).				
IT	161693-70-5P				

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(phospholipid-ligand conjugates for enhancing liposomal delivery system)

RN 161693-70-5 CAPLUS

CN 8,10,14-Trioxa-5-aza-9-phosphadriacontanoic acid, 9-hydroxy-4,15-dioxo-12-[(1-oxooctadecyl)oxy]-, 9-oxide (9CI) (CA INDEX NAME)



L10 ANSWER 20 OF 30 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1995:352310 CAPLUS

DN 122:196706

TI Folate-mediated tumor cell targeting of liposome-entrapped doxorubicin in vitro

AU Lee, Robert J.; Low, Philip S.

CS Department of Chemistry, Purdue University, West Lafayette, IN, 47907, USA

SO Biochimica et Biophysica Acta, Biomembranes (1995), 1233(2), 134-44

CODEN: BBBMBS; ISSN: 0005-2736

PB Elsevier B.V.

DT Journal

LA English

AB Receptors for the vitamin folic acid are frequently overexpressed on epithelial cancer cells. To examine whether this overexpression might be exploited to specifically deliver liposome-encapsulated drug mols. in vitro, folate-targeted liposomes were prepared by incorporating 0.1 mol% of a folate-polyethylene glycol-distearoylphosphatidylethanolamine (folate-PEG-DSPE) construct into the lipid bilayer, and were loaded with doxorubicin (DOX), an anticancer drug. Uptake of folate-PEG-liposomal DOX by KB cells was 45-fold higher than that of non-targeted liposomal DOX, and 1.6-times higher than that of free DOX, while the cytotoxicity was 86 and 2.7-times higher, resp. Folate-targeting is fully compatible with PEG-coating of the liposomes, since incorporation of 4 mol% PEG2000-DSPE does not reduce the uptake or cytotoxicity of folate-PEG-liposomal DOX. Uptake of folate-PEG-liposomes was inhibited by 1 mM free folic acid but was unaffected by physiol. concns. of folate. In HeLa/WI38 co-cultures, folate-PEG-liposomes encapsulating calcein, a fluorescent dye, were found to be almost exclusively internalized by the HeLa cells which overexpress the folate receptors. Thus, it is suggested that folate targeting constitutes a possible mechanism for improving the specificity of PEG-coated liposomes for cancer cells.

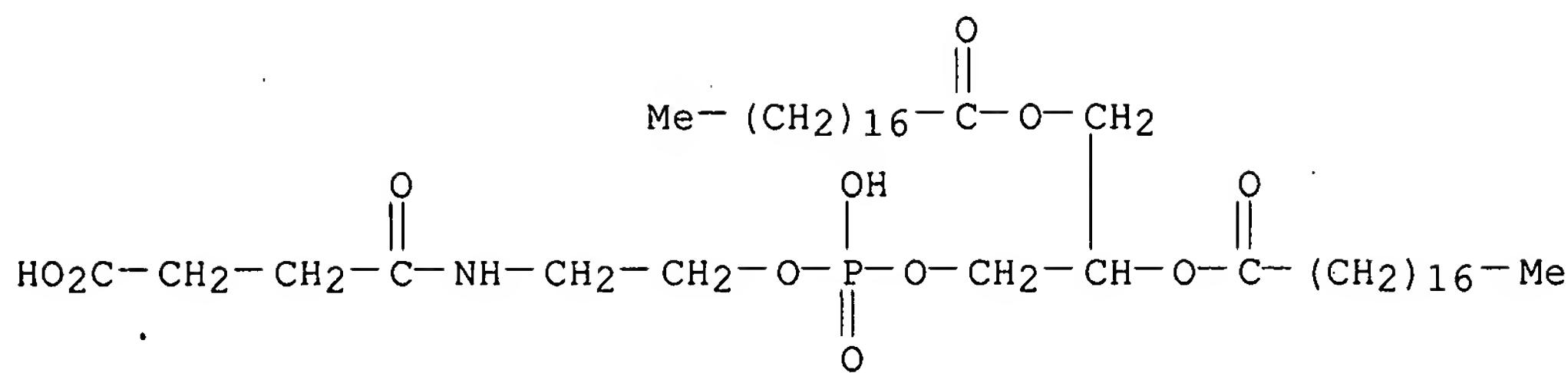
IT 161693-70-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(folate-mediated targeting of doxorubicin encapsulated in PEG-coated liposomes)

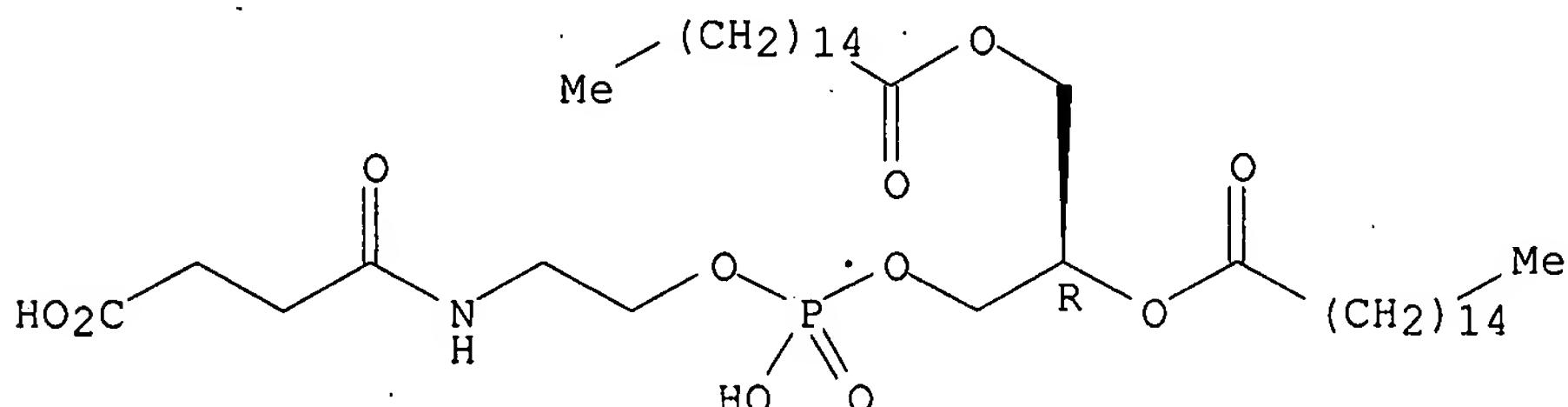
RN 161693-70-5 CAPLUS

CN 8,10,14-Trioxa-5-aza-9-phosphadriacontanoic acid, 9-hydroxy-4,15-dioxo-12-[(1-oxooctadecyl)oxy]-, 9-oxide (9CI) (CA INDEX NAME)



L10 ANSWER 21 OF 30 CAPLUS COPYRIGHT 2007 ACS on STN  
AN 1994:650457 CAPLUS  
DN 121:250457  
TI Synthesis and Characterization of Chelator-Lipids for Reversible Immobilization of Engineered Proteins at Self-Assembled Lipid Interfaces  
AU Schmitt, Lutz; Dietrich, Christian; Tampe, Robert  
CS Physik Department, Technische Universitaet Muenchen, Garching, D-85747, Germany  
SO Journal of the American Chemical Society (1994), 116(19), 8485-91  
CODEN: JACSAT; ISSN: 0002-7863  
DT Journal  
LA English  
OS CASREACT 121:250457  
AB In mol. biol. and protein engineering, immobilized metal ion affinity chromatog. (IMAC) using a NTA-chelator is a very powerful technique in identification and isolation of oligo-histidine-tagged fusion proteins. This concept was transferred to the properties of self-assembling systems with the aim of reversible immobilization, orientation of biomols., and functionalization of lipid interfaces. Here are described the synthesis and the chemical and phys. characterization of such metal affinity lipids. The NTA-chelator was coupled either to a phospholipid, DPPE, or to a synthetic lipid, dioctadecylamine. Metal complex formation was investigated by TLC and FTIR techniques. Using film balance techniques the generation of metal sensitive lipid films is demonstrated. In the presence of Ni<sup>2+</sup> drastic changes of the area-pressure isotherms were observed. Furthermore, the specific ligand binding of imidazole as a model compound for oligo-histidine-tagged fusion proteins to these functionalized metal-lipid films was investigated.  
IT 150525-42-1P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
RN 150525-42-1 CAPLUS  
CN 8,10,14-Trioxa-5-aza-9-phosphatriacontanoic acid, 9-hydroxy-4,15-dioxo-12-[(1-oxohexadecyl)oxy]-, 9-oxide, (12R)- (CA INDEX NAME)

## Absolute stereochemistry.

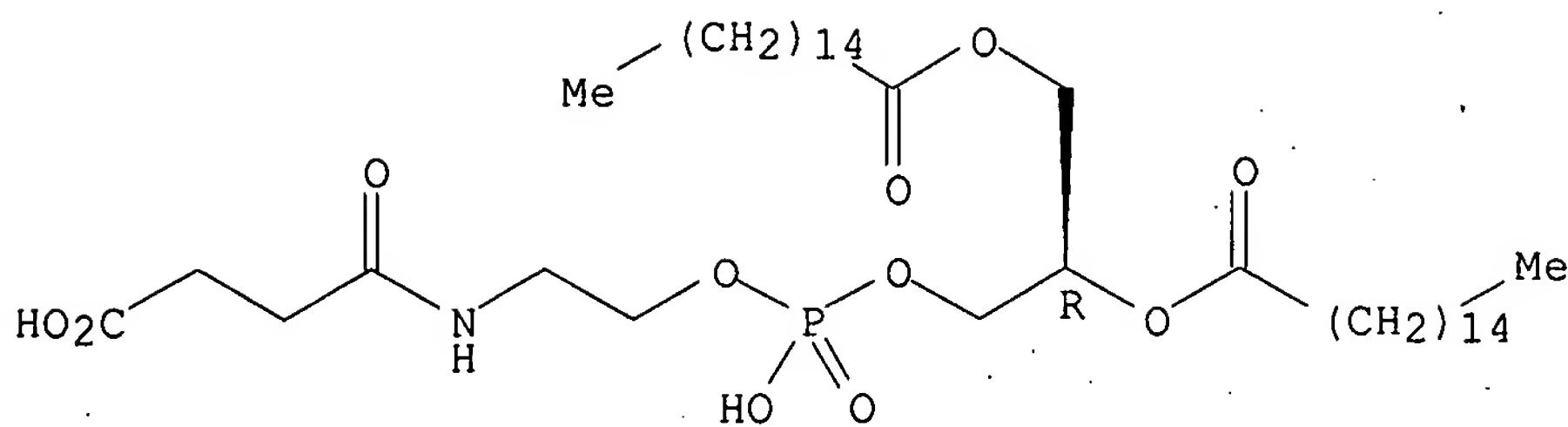


L10 ANSWER 22 OF 30 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1993:603859 CAPLUS  
 DN 119:203859  
 TI Preparation of lipid conjugates of therapeutic peptides and protease inhibitors  
 IN Basava, Channa; Hostetler, Karl Y.  
 PA Vical, Inc., USA  
 SO PCT Int. Appl., 72 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9301828	A1	19930204	WO 1992-US6153	19920722
	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
	US 5554728	A	19960910	US 1991-734434	19910723
	CA 2113156	A1	19930204	CA 1992-2113156	19920722
	AU 9224251	A	19930223	AU 1992-24251	19920722
	AU 671078	B2	19960815		
	EP 596024	A1	19940511	EP 1992-917096	19920722
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE				
	JP 07501316	T	19950209	JP 1992-503064	19920722
	US 5804552	A	19980908	US 1995-458401	19950602
PRAI	US 1991-734434	A	19910723		
	WO 1992-US6153	A	19920722		
OS	MARPAT 119:203859				
AB	Title compds., comprising therapeutic peptides, including human immunodeficiency virus (HIV) protease inhibitors covalently linked to phospholipids, glycerides, or other membrane-targeting and membrane-anchoring species, and their pharmaceutically acceptable salts, together with processes for their preps., are described. The invention also provides novel HIV protease inhibitors. The prepared compds. possess useful pharmacol. properties, such as antiviral activity towards viral infection and inhibitory activity towards viral proteases. Therefore, these compds. can be used in the prophylaxis or treatment of viral infections, in particular infections caused by HIV or other retroviruses. The targeting technol. as described for the protease inhibitors is also applicable to a variety of inhibitors of other enzymes. Thus, R-Ala-Ala-D-β-Nal-Pip-OMe (I; R = Ac, β-Nal = β-naphthylalanine, Pip = pipecolic acid), prepared by standard solid-phase methods, had IC <sub>50</sub> >100 μM in an antiviral assay, while dipalmitoylglycerophosphatidylethanolamine conjugate I [R = (R)-Me(CH <sub>2</sub> ) <sub>14</sub> CO <sub>2</sub> CH[CH <sub>2</sub> O <sub>2</sub> C(CH <sub>2</sub> ) <sub>14</sub> Me]CH <sub>2</sub> OP(O)(OH)OCH <sub>2</sub> CH <sub>2</sub> NHCOCH <sub>2</sub> CH <sub>2</sub> CO], prepared via coupling of succinylated ethanolamine derivative ROH with the corresponding peptide, had IC <sub>50</sub> = 10 μM.				
IT	150525-42-1P 150525-43-2P				
	RL: SPN (Synthetic preparation); PREP (Preparation)				
	(preparation and amidation reactions of, with peptides, in preparation of lipid conjugate protease inhibitors)				
RN	150525-42-1 CAPLUS				
CN	8,10,14-Trioxa-5-aza-9-phosphatriacontanoic acid, 9-hydroxy-4,15-dioxo-12-[(1-oxohexadecyl)oxy]-, 9-oxide, (12R)- (CA INDEX NAME)				

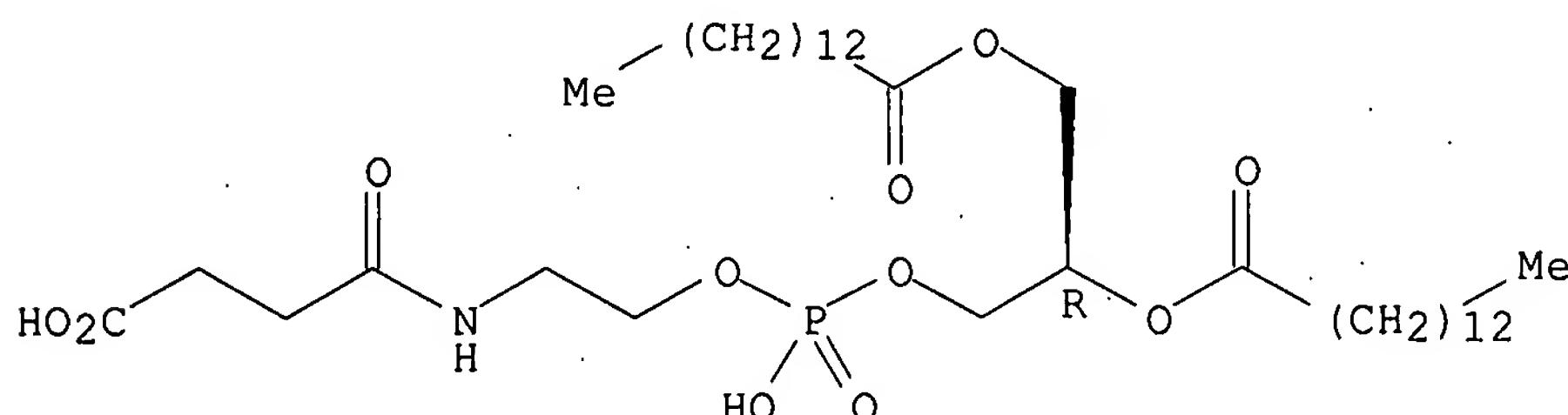
Absolute stereochemistry.



RN 150525-43-2 CAPLUS

CN 8,10,14-Trioxa-5-aza-9-phosphaoctacosanoic acid, 9-hydroxy-4,15-dioxo-12-[(1-oxotetradecyl)oxy]-, 9-oxide, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L10 ANSWER 23 OF 30 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1993:249864 CAPLUS

DN 118:249864

TI Interbilayer transfer of phospholipid-anchored macromolecules via monomer diffusion

AU Silvius, John R.; Zuckermann, Martin J.

CS Dep. Biochem., McGill Univ., Montreal, QC, H3G 1Y6, Can.

SO Biochemistry (1993), 32(12), 3153-61

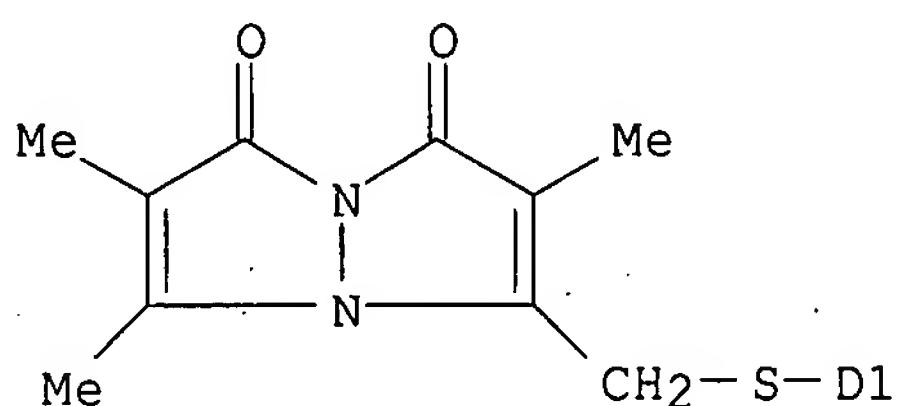
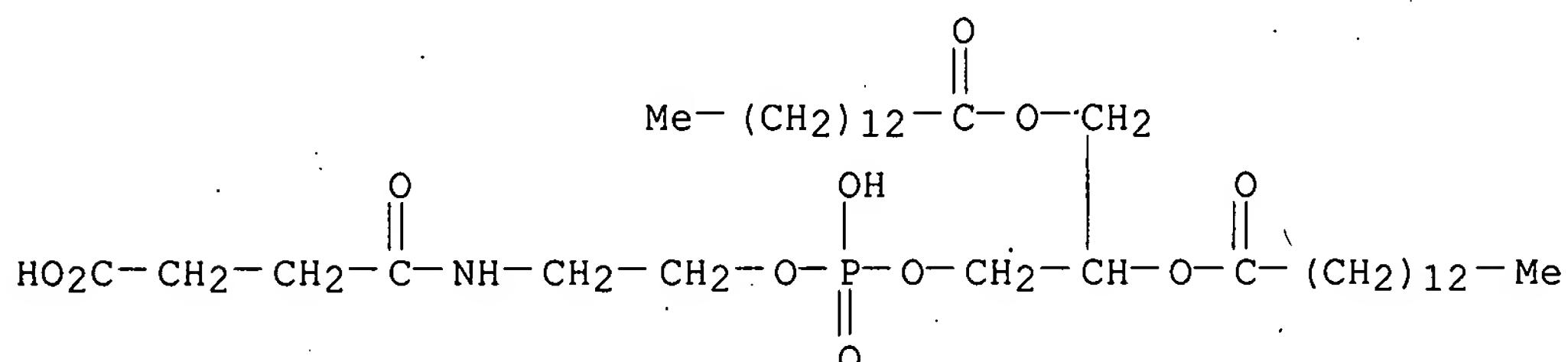
CODEN: BICHAW; ISSN: 0006-2960

DT Journal

LA English

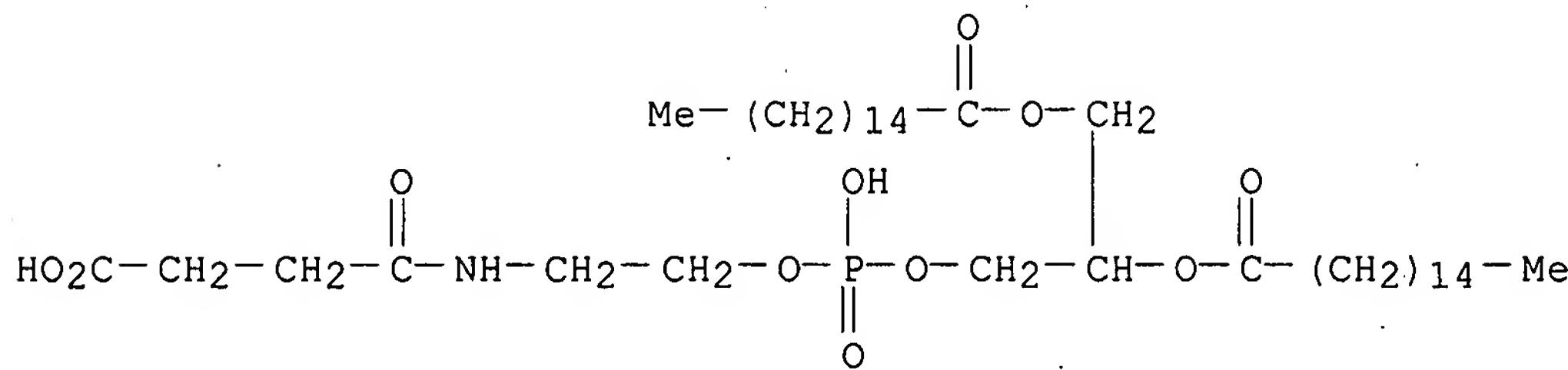
AB A series of conjugates was prepared by linking various hydrophilic macromols. [poly(ethylene glycols), polylysine, aminodextrans, or apotransferrin] to synthetic phosphatidylethanolamines via linker moieties incorporating a fluorescent bimane group. Using a fluorescence energy transfer-based assay, the rate of transfer of these species between phospholipid vesicles was monitored as a function of the nature and size of the coupled macromol. and of the acyl chain composition of the lipid anchor. Conjugates in which the phospholipid anchor is linked to a small hydrophilic terminal residue (e.g., ethanolamine or ethylenediamine) transfer between large unilamellar vesicles of egg phosphatidylcholine with half-times ranging from tens of minutes (for dimyristoyl lipid conjugates) to a few tens of hours (for dipalmitoyl and 1-palmitoyl-2-oleoyl lipid conjugates), in agreement with previous results for unlabeled phospholipids. Conjugation of these same lipid anchors to larger hydrophilic mols. markedly accelerates their rates of intermembrane transfer, by factors ranging from 5-7-fold (for conjugates with apotransferrin and aminodextrans of mol. weight 10,000-70,000) to over 25-fold [for conjugates with poly(ethylene glycol)-5000]. In all cases the observed transfer appears to reflect the diffusion of lipid monomers through the aqueous phase. These results suggest that substantial intermembrane transfer can occur, on a time scale of several hours or less, for hydrophilic macromols. conjugated to diacyl(/alkyl) lipids with 14- to 18-carbon chains unless portions of the conjugate other than the lipid anchors also interact strongly with the membrane.

IT 147793-19-9P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and reaction with amines and interbilayer transfer of)  
RN 147793-19-9 CAPLUS  
CN Tetradecanoic acid, 1-[10-carboxy-3-hydroxy-3-oxido-8-oxo-9(or 10)-[[[2,5,6-trimethyl-1,7-dioxo-1H,7H-pyrazolo[1,2-a]pyrazol-3-yl)thio)methyl]-2,4-dioxa-7-aza-3-phosphadec-1-yl]-1,2ethanediyl ester (9CI) (CA INDEX NAME)



L10 ANSWER 24 OF 30 CAPLUS COPYRIGHT 2007 ACS on STN  
AN 1992:200949 CAPLUS  
DN 116:200949  
TI Influence of the galactosyl ligand structure on the interaction of galactosylated liposomes with mouse peritoneal macrophages  
AU Haensler, Jean; Schuber, Francis  
CS Fac. Pharm., Univ. Louis Pasteur, Illkirch, 67041, Fr.  
SO Glycoconjugate Journal (1991), 8(2), 116-24  
CODEN: GLJOEW; ISSN: 0282-0080  
DT Journal  
LA English  
AB Liposomes bearing at their surface mono- and triantennary galactosyl ligands were prepared and their interaction with the galactose receptor of mouse peritoneal macrophages studied. Triantennary structures were synthesized by coupling derivs. of 1-thio- $\beta$ -D-galactose to the amino groups of lysyl-lysine dipeptide. Galactosyl liposomes were obtained either by synthesis of neo-galactolipids followed by their incorporation into the vesicles or by neo-galactosylation of preformed liposomes by reaction between thiol-functionalized galactosyl ligands and vesicles bearing maleimido groups. The interaction of the galactosylated liposomes with the macrophage lectin was remarkably sensitive to the topol. of the ligands, i.e., a spacer-arm length about 3 nm was necessary and, in contrast to results obtained with the galactose receptor of other cells, the triantennary structure did not provide addnl. binding. Related to the strategy of drug delivery with targeted liposomes, these results indicate that lectins from different cells might possibly be distinguished by using multiantennary ligands having optimal geometries.  
IT 88848-80-0  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction of, with galactose derivs., interaction with peritoneal macrophages in liposomes in relation to)  
RN 88848-80-0 CAPLUS

CN 8,10,14-Trioxa-5-aza-9-phosphatricacontanoic acid, 9-hydroxy-4,15-dioxo-12-[(1-oxohexadecyl)oxy]-, 9-oxide (9CI) (CA INDEX NAME)



L10 ANSWER 25 OF 30 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1991:627813 CAPLUS

DN 115:227813

TI Carboxyacyl derivatives of phospholipid, and carbodiimide method for sensitizing liposome with antigen or antibody for liposome lysis immunoassay

IN Umeda, Mamoru; Kobayashi, Reiji

PA Nissui Seiyaku Co., Ltd., Japan

SO Jpn. Kokai Tokkyo Koho, 7 pp.

CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI JP 03073856	A	19910328	JP 1989-209789	19890814
PRAI JP 1989-209789		19890814		

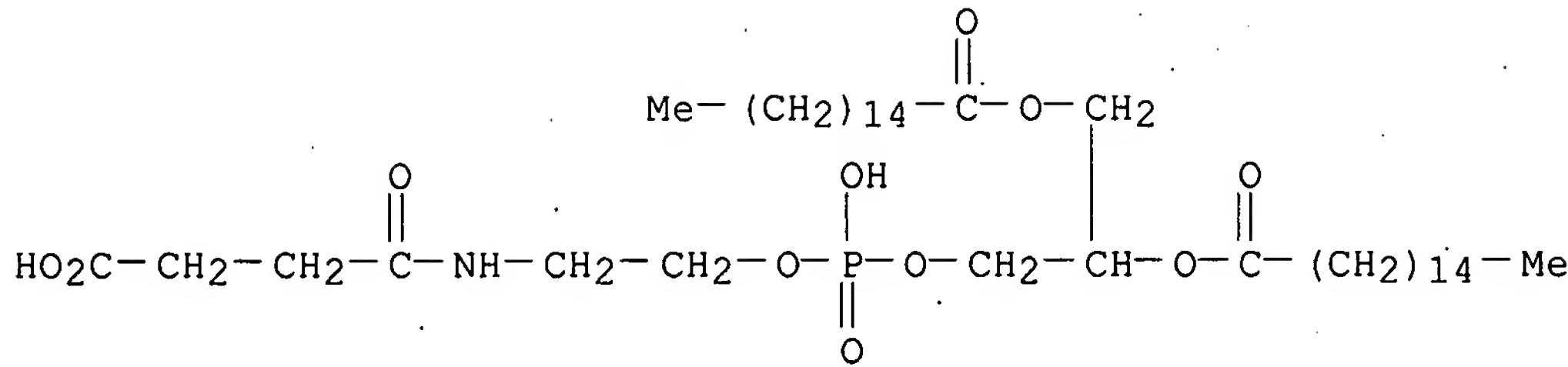
AB Carboxyacyl derivs. of phospholipid are used to introduce antigen or antibody to the surface of liposome which encapsulates a hydrophilic label for liposome lysis immunoassay for diagnosing endocrine disease. With the liposome, the immunoassay is simple and sensitive, and is not influenced by complement interference, i.e. antigen-antibody complex formation-independent lysis. Thus, N-succinyl, glutamyl, adipoyl, pimeloyl, suberyl, sebaciroyl, (11-carboxyimidecanoyl), and (13-carboxytridecanoyl) dipalmitoylphosphatidylethanolamine were prepared from dipalmitoyl phosphatidylethanolamine and succinic; glutaric; adipic; pimelic; suberic; sebacic; decadicarboxylic; and dodecanedicarboxylic anhydrides, and were used to link anti-C-reactive protein (CRP) IgG with liposome by adding ethyldimethylpropylaminocarbodiimide. The IgG sensitized liposome was then used for CRP determination in human blood.

IT 88848-80-0P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, for sensitizing liposome with antigen or antibody via carbodiimide, for preventing complement interference in liposome lysis immunoassay)

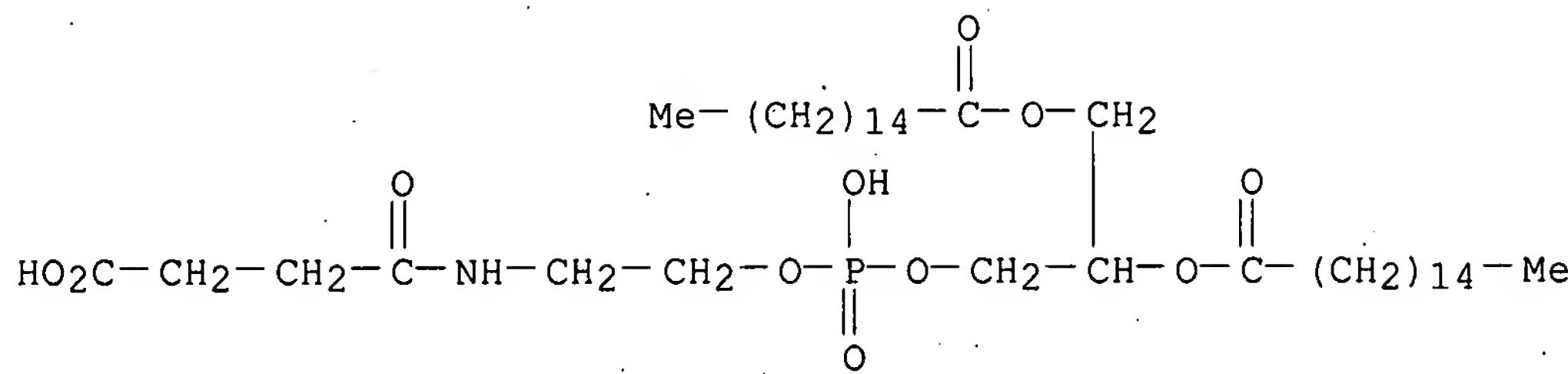
RN 88848-80-0 CAPLUS

CN 8,10,14-Trioxa-5-aza-9-phosphatricacontanoic acid, 9-hydroxy-4,15-dioxo-12-[(1-oxohexadecyl)oxy]-, 9-oxide (9CI) (CA INDEX NAME)



L10 ANSWER 26 OF 30 CAPLUS COPYRIGHT 2007 ACS on STN  
AN 1990:154774 CAPLUS  
DN 112:154774  
TI Method for preparing phosphodiester conjugates useful for preparing immunoactive liposomes.  
IN Law, Say Jong  
PA Ciba Corning Diagnostics Corp., USA  
SO Eur. Pat. Appl., 8 pp.  
CODEN: EPXXDW  
DT Patent  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 307175	A2	19890315	EP 1988-308254	19880907
	EP 307175	A3	19900328		
	EP 307175	B1	19950322		
	R: AT, BE, CH, DE, ES, FR, GB, IT, LI CA 1340413 JP 01107152 JP 08007218 AT 120276 ES 2071618	C A B T T3	19990302 19890425 19960129 19950415 19950701	CA 1988-571365 JP 1988-224362 AT 1988-308254 ES 1988-308254	19880707 19880907 19880907 19880907 19880907
PRAI	US 1987-94667	A	19870909		
OS	MARPAT 112:154774				
AB	A method for preparing a phosphodiester-ligand-analyte conjugate comprises reacting a polar phospholipid R1CH2CHR2CH2OP(:O)(OH)OR3 [R1, R2 = H, OH, R', OR'; R' = C1-24 (un)saturated, (un)branched alkyl or alkylene; R3 = C1-24 (un)branched alkylamine] with a ligand (reactive at R3) and reacting this conjugate with an analyte (preferably thyroxine or triiodothyronine) through the ligand. The final conjugate can be used to form liposomes for use in immunoassays. Thus, phosphatidylethanolamine succinate (PE-Suc) was formed from the reaction of (1,2-dipalmitoyl-3-rac-phosphatidyl)ethanolamine 440 with succinic anhydride 76 mg and triethylamine 0.09 mL in 40 mL HCONMe <sub>2</sub> :CHCl <sub>3</sub> (1:1) for 1.5 h at 65°. PE-Suc 402 mg in CHCl <sub>3</sub> was then reacted with triethylamine 100 μL, followed by Et chlorformate 65 μL, L-thyroxine (T4) Na salt 406 mg, and DMF 10 mL at 0°. The PE-Suc-T4 conjugate was purified by TLC and 0.95 mg was combined in CHCl <sub>3</sub> with L-dipalmitoylphosphatidylcholine 125, cholesterol 67.5, and L-dipalmitoylphosphatidylglycerol 11.5 mg to form a dry lipid film which was mixed with glucose-6-phosphate dehydrogenase (37.5 kilounits) in 2% glycerol to form liposomes which were used in an enzyme membrane immunoassay.				
IT	88848-80-0P				
	RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of, in liposome preparation for immunoassays)				
RN	88848-80-0 CAPLUS				
CN	8,10,14-Trioxa-5-aza-9-phosphatriacontanoic acid, 9-hydroxy-4,15-dioxo-12-[(1-oxohexadecyl)oxy]-, 9-oxide (9CI) (CA INDEX NAME)				



L10 ANSWER 27 OF 30 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1986:438652 CAPLUS

DN 105:38652

TI Use of phosphotriester synthetic methods for preparation of  
phosphatidylethanolamine-analyte conjugates

AU Law, Say Jong; Myles, Arthur

CS Dep. Mol. Biol. Immunol., Collaborative Res., Inc., Lexington, MA, 02173,  
USA

SO Tetrahedron Letters (1986), 27(3), 271-4

CODEN: TELEAY; ISSN: 0040-4039

DT Journal

## LA English

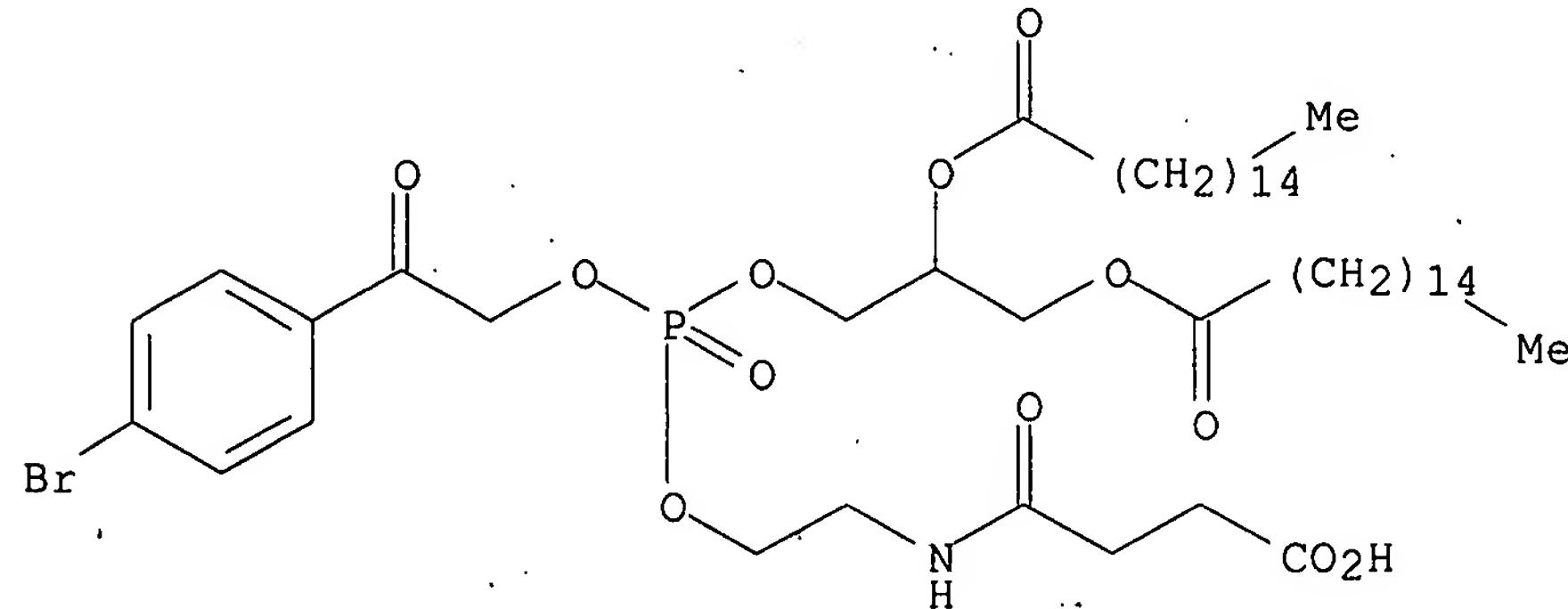
AB Amphiphilic phosphatidylethanolamine conjugates of therapeutically or biol. active analytes were prepared by using a new phosphotriester synthetic approach and used for functionalization of liposomes. Protected phosphatidylethanolamine phosphotriester intermediates were prepared and directly coupled to penicillin G and indirectly coupled via a succinamide ligand, to L-thyroxine. The deprotected conjugates were used for preparation of analyte functionalized liposomes which form the basis of highly reproducible and sensitive assays for penicillin and thyroxine.

IT 94451-77-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
· (Reactant or reagent)  
· (preparation and reaction with thyroxine)

RN 94451-77-1 CAPLUS  
SN 8 10 14 Triplex F 2

CN 8,10,14-Trioxa-5-aza-9-phosphatriacontanoic acid, 9-[2-(4-bromophenyl)-2-oxoethoxy]-4,15-dioxo-12-[(1-oxohexadecyl)oxy]-, 9-oxide (9CI) (CA INDEX NAME)



L10 ANSWER 28 OF 30 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1985:58884 CAPLUS

DN 102:58884

TI Use of phosphotriester intermediates for preparation of functionalized liposomes

IN Myles, Arthur; Law, Say Jong; Cole, Frank X.

PA Collaborative Research, Inc., USA

SO U.S., 12 pp.  
CODEN: USXXAM

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 4480041	A	19841030	US 1982-396678	19820709
PRAI US 1982-396678		19820709		
OS MARPAT 102:58884				

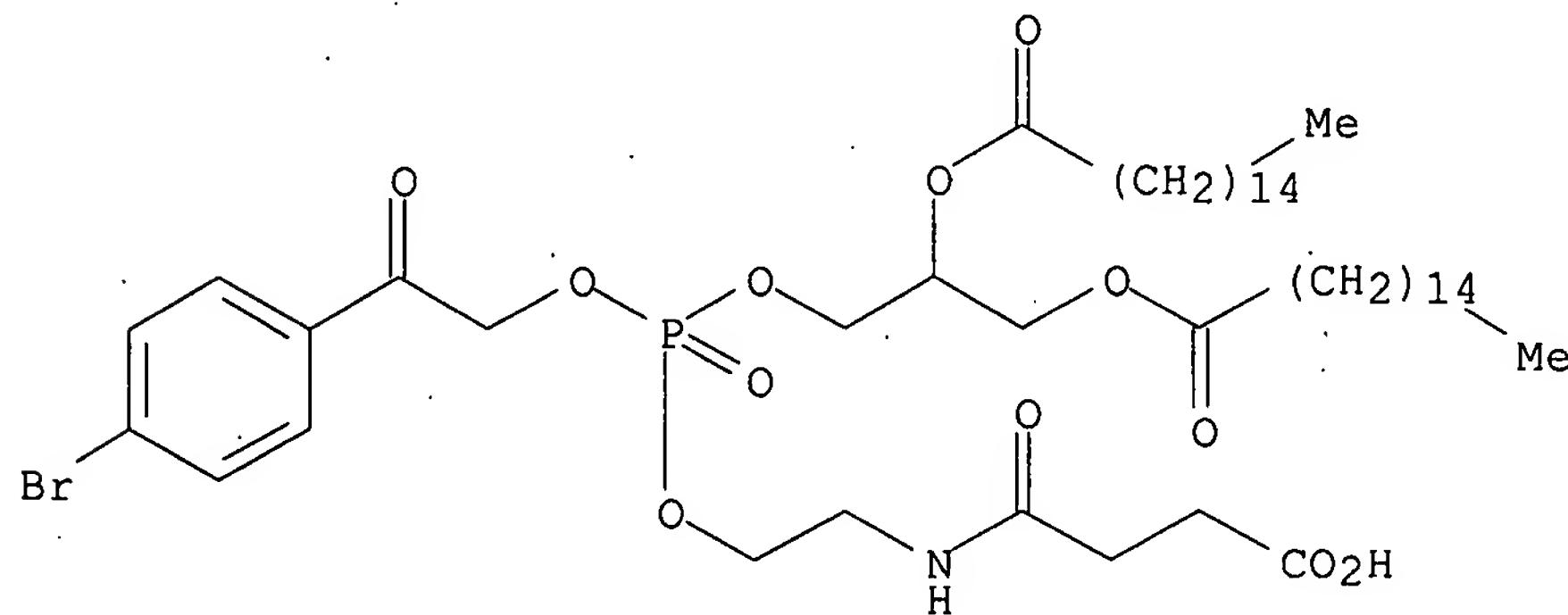
AB Liposomes covalently labeled with analytes (e.g., antibiotics, drugs, hormones, other antigens) on their outer surfaces and containing entrapped enzymes are prepared for enzyme-membrane immunoassays (liposome immunoassays) by using phospholipids derivatized with the desired analyte (or with a ligand spacer and analyte) which are prepared via phosphotriester intermediates. int: the derivatized phospholipids can be prepared in multigram quantities and then incorporated into the liposomes. Natural or synthetic amphiphilic phospholipids, and especially phosphatidylethanolamines, may be used as starting materials. Thus, for the determination of T4,  $\beta,\gamma$ -dipalmitoyl-DL- $\alpha$ -phosphatidylethanolamine was protected with the BOC (tert-butoxycarbonyl) group, and the protected product was treated with  $\alpha,p$ -dibromoacetophenone to form the triester N-tert-butoxycarbonyl- $\beta,\gamma$ -dipalmitoyl-DL- $\alpha$ -phosphatidylethanolamine 2-(4-bromophenyl)-2-oxoethyl ester. The latter compound was deprotected, and the deprotected product then was treated with succinic anhydride to form N-succinyl- $\beta,\gamma$ -dipalmitoyl-DL- $\alpha$ -phosphatidylethanolamine 2-(4-bromophenyl)-2-oxoethyl ester which was treated with L-T4 to give a conjugate. The conjugate, after removal of the 2-(4-bromophenyl)-2-oxoethyl group, gave the desired T4-derivatized phosphatidylethanolamine. The latter compound was used along with lecithin and cholesterol to prepare liposomes that were loaded with alkaline phosphatase and used for the determination of T4 by immunoassay.

IT 94451-77-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and reaction of, with thyroxine)

RN 94451-77-1 CAPLUS

CN 8,10,14-Trioxa-5-aza-9-phosphatriacontanoic acid, 9-[2-(4-bromophenyl)-2-oxoethoxy]-4,15-dioxo-12-[(1-oxohexadecyl)oxy]-, 9-oxide (9CI) (CA INDEX NAME)



L10 ANSWER 29 OF 30 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1984:83795 CAPLUS

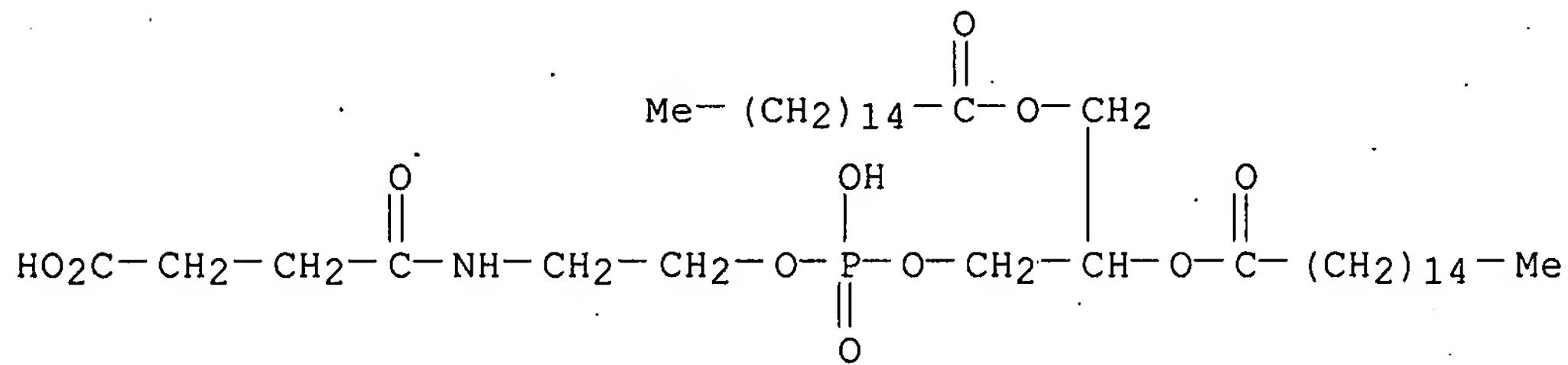
DN 100:83795

TI An alternative procedure for the preparation of immunogenic liposomal model membranes

AU Kinsky, Stephen C.; Loader, Joan E.; Benson, Amy L.

CS Dep. Pediatr., Natl. Jew. Hosp., Denver, CO, 80206, USA

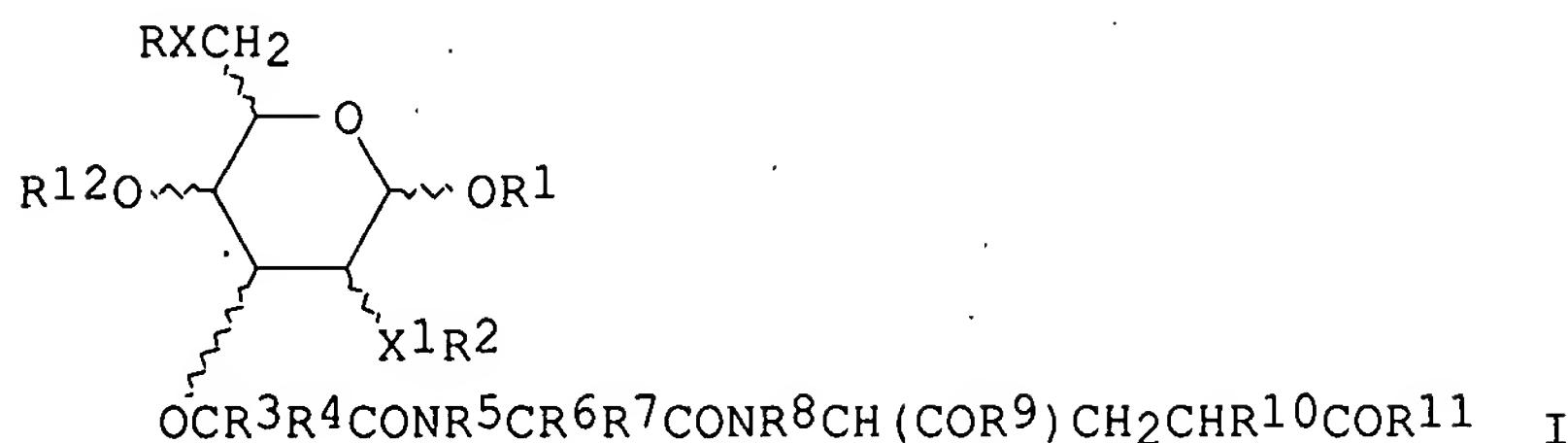
SO Journal of Immunological Methods (1983), 65(3), 295-306  
 CODEN: JIMMBG; ISSN: 0022-1759  
 DT Journal  
 LA English  
 AB A new procedure for the preparation of immunogenic liposomes is described which circumvents the need to synthesize the N-(hapten)-substituted derivs. of phosphatidylethanolamine that were previously employed for this purpose. The method is based on the generation of liposomes containing the N-hydroxysuccinimide (NHS) esters of either palmitic acid, cholesteryl-hemisuccinate, or N-succinyl-phosphatidylethanolamine. Reaction of these performed liposomes with a hapten that possesses a substitutable amino group [e.g., dinitrophenyl (DNP)-lysine] results in covalent attachment of the hapten to the plaque-forming cells in mice. The reliability of this procedure is indicated by the fact that these liposomes share the essential immunol. properties of liposomes sensitized by incorporation of N-substituted phosphatidylethanolamine derivs. The magnitude of the response was dependent on: (a) the presence of lipid A in the liposomes; (b) the phospholipid composition of the liposomes; (c) the distance separating the DNP determinant from the liposomal surface. Addnl. applications of liposomes, which contain the NHS esters, are discussed.  
 IT 88848-80-0P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
     (preparation of)  
 RN 88848-80-0 CAPLUS  
 CN 8,10,14-Trioxa-5-aza-9-phosphatriacontanoic acid, 9-hydroxy-4,15-dioxo-12-[(1-oxohexadecyl)oxy]-, 9-oxide (9CI) (CA INDEX NAME)



L10 ANSWER 30 OF 30 CAPLUS COPYRIGHT 2007 ACS on STN  
 AN 1983:54497 CAPLUS  
 DN 98:54497  
 TI Phosphorylated derivatives, pharmaceutical compositions containing such derivatives, and their use  
 IN Baschang, Gerhard; Hartmann, Albert; Wacker, Oskar; Tarcsay, Lajos  
 PA Ciba-Geigy A.-G. , Switz.  
 SO Eur. Pat. Appl., 182 pp.  
 CODEN: EPXXDW  
 DT Patent  
 LA German  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 56992	A1	19820804	EP 1982-100445	19820122
	R: AT, BE, CH, DE, FR, IT, LU, NL, SE				
US	4423038	A	19831227	US 1982-340680	19820119
FI	8200178	A	19820724	FI 1982-178	19820120
GB	2092591	A	19820818	GB 1982-1709	19820121
GB	2092591	B	19840704		
ES	508944	A1	19840701	ES 1982-508944	19820121
CA	1190221	A1	19850709	CA 1982-394632	19820121
DK	8200282	A	19820724	DK 1982-282	19820122
NO	8200200	A	19820726	NO 1982-200	19820122

NO 152904	B	19850902		
NO 152904	C	19851211		
AU 8279751	A	19820729	AU 1982-79751	19820122
JP 57142996	A	19820903	JP 1982-8742	19820122
ZA 8200433	A	19821229	ZA 1982-433	19820122
DD 202169	A5	19830831	DD 1982-236918	19820122
HU 26858	A2	19830928	HU 1982-189	19820122
IL 64847	A	19860228	IL 1982-64847	19820122
ES 522435	A1	19850101	ES 1983-522435	19830516
ES 528142	A1	19860416	ES 1983-528142	19831216
PRAI CH 1981-439	A	19810123		
OS MARPAT 98:54497				
GI				



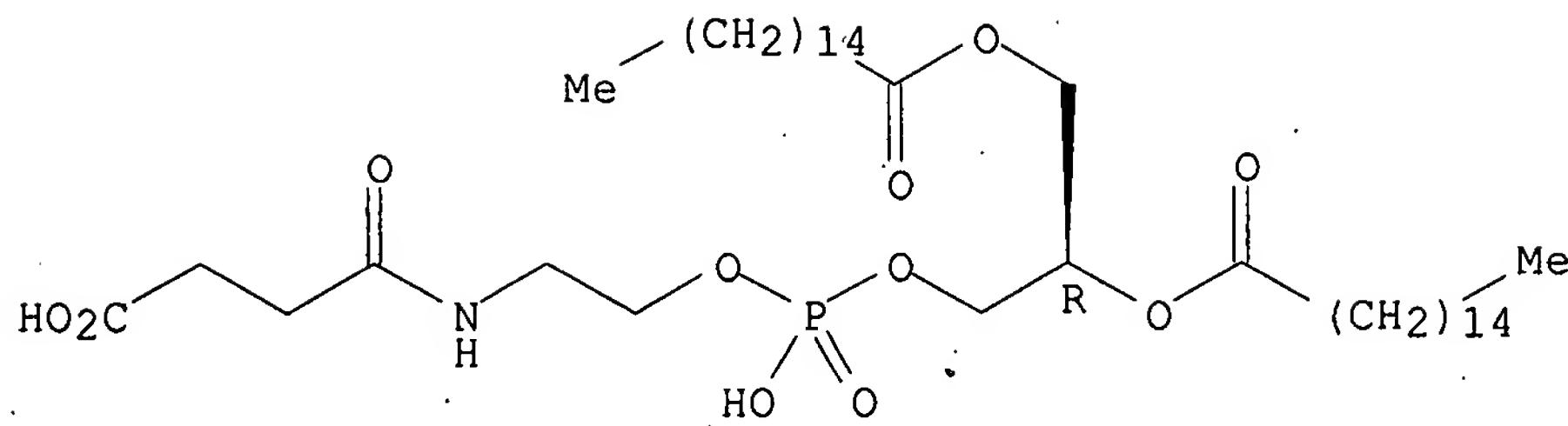
AB Glycopeptides I [X, X1 = O, NR13 (R13 = H, alkyl); R, R1, R2, R12 = (Z1Z2)nR14 [Z = CO, CS; Z1 = (un)substituted alkylene; Z2 = O, NR13; R14 = P(O)(OH)OR15 (R15 = aliphatic or cycloaliphatic group with  $\geq 7$  C atoms), P(O)(OH)OCHR16R17. [R16 = H; R17 = CH<sub>2</sub>CH<sub>2</sub>OH, CH(OH)CH<sub>2</sub>OH; R16, R17 = esterified or etherified CH<sub>2</sub>OH]; n = 0, 1]; R3, R4, R5, R7, R8 = H, alkyl; R6 = H, alkyl, X2(Z3Z4Z5)mR18 [X2 = O, S, NR13; Z3 = CO, CS; Z4 = (un)substituted alkylene; Z5 = O, NR13, R18 = P(O)(OH)OR15, P(O)(OH)OCHR16R17; m = 0, 1]; R5R6 = 1,3- or 1,4-alkylene; R9, R11 = Z6Z7Z8R19 [Z6 = O, S, NR13, Z7 = (un)substituted alkylene; Z8 = O, NR13; R19 = P(O)(OH)OR15, P(O)(OH)OCHR16R17]; R10 = H, free or esterified or amidated CO<sub>2</sub>H] were prepared as immunomodulators. Thus, N-acetylnormuramyl-L-alanyl-D-isoglutamine was esterified with Ph<sub>2</sub>C:N<sub>2</sub> to give the corresponding  $\gamma$ -diphenylmethyl ester, which was acylated with succinic anhydride to give the corresponding 6-O-succinoyl derivative, which was esterified with N-hydroxysuccinimide by DCC to give the corresponding succinimido ester. The latter was condensed with 2-(1,2-dipalmitoyl-sn-glycero-3-hydroxyphosphoryloxy)ethylamine to give a product, which had its diphenylmethyl ester cleaved by hydrogenolysis over Pd/BuSO<sub>4</sub> to give N-acetyl-6-O-[(N-2-(1,2-dipalmitoyl-sn-glycero-3-hydroxyphosphoryloxy)ethyl)succinamoyl]normuramyl-L-alanyl-D-isoglutamine.

IT 84228-13-7P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and reaction of, with muramyl dipeptide derivative)

RN 84228-13-7 CAPLUS  
CN 8,10,14-Trioxa-5-aza-9-phosphatriacontanoic acid, 9-hydroxy-4,15-dioxo-12-[(1-oxohexadecyl)oxy]-, 9-oxide, sodium salt, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> file registry	SINCE FILE	TOTAL
COST IN U.S. DOLLARS	ENTRY	SESSION
FULL ESTIMATED COST	159.98	691.00
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
CA SUBSCRIBER PRICE	ENTRY	SESSION
	-23.40	-24.18

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 DICTIONARY FILE UPDATES: 20 JUN 2007 HIGHEST RN 938114-25-1

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=>  
 Uploading C:\Documents and Settings\jcho2\My Documents\10549630-m.str

L11        STRUCTURE UPLOADED

=> d 111  
 L11 HAS NO ANSWERS  
 L11        STR

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

Structure attributes must be viewed using STN Express query preparation.

=> s l11 sss full

FULL SEARCH INITIATED 11:09:05 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 1340 TO ITERATE

100.0% PROCESSED 1340 ITERATIONS

SEARCH TIME: 00.00.01

L12 10 SEA SSS FUL L11

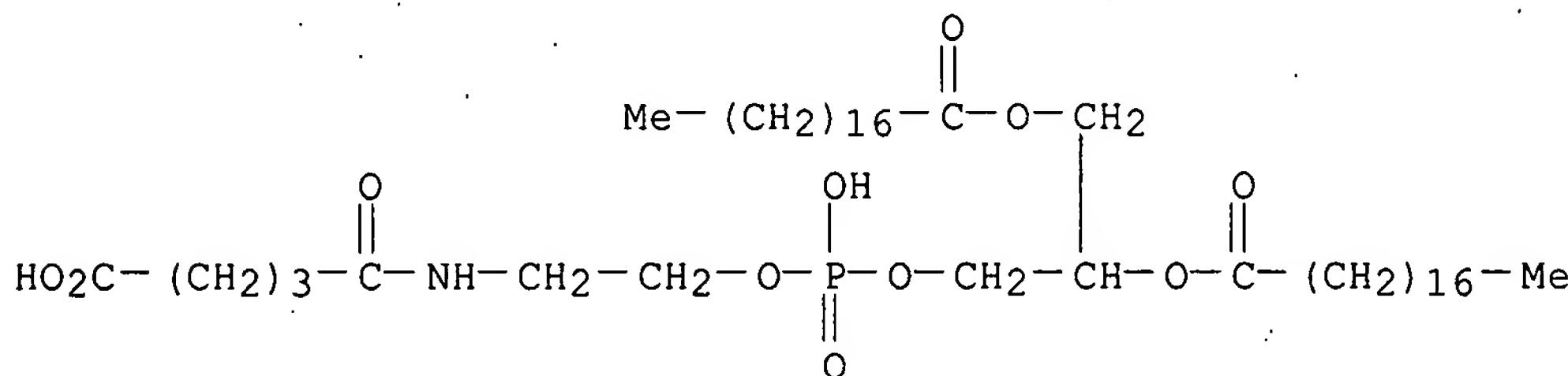
=> d scan

L12 10 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 9,11,15-Trioxa-6-aza-10-phosphatritriacontanoic acid, 10-hydroxy-5,16-dioxo-13-[(1-oxooctadecyl)oxy]-, 10-oxide, ester with octaglycerol (9CI)

MF C46 H88 N O11 P . x C24 H50 O17

CM 1



CM 2

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):end

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE

FULL ESTIMATED COST

ENTRY

TOTAL

SESSION

172.10

863.10

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

CA SUBSCRIBER PRICE

ENTRY

TOTAL

0.00

SESSION

-24.18

FILE 'CAPLUS' ENTERED AT 11:09:20 ON 21 JUN 2007

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FILE COVERS 1907 - 21 Jun 2007 VOL 146 ISS 26

FILE LAST UPDATED: 20 Jun 2007 (20070620/ED)

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<http://www.cas.org/infopolicy.html>

=> s 112

L13 21 L12

=> d 113 1-21 bib abs hitstr

L13 ANSWER 1 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2007:82183 CAPLUS

DN 146:333479

TI DNA-Oligonucleotide Encapsulating Liposomes as a Secondary Signal Amplification Means

AU Edwards, Katie A.; Baeumner, Antje J.

CS Department of Biological and Environmental Engineering, Cornell University, Ithaca, NY, 14853, USA

SO Analytical Chemistry (2007), 79(5), 1806-1815  
CODEN: ANCHAM; ISSN: 0003-2700

PB American Chemical Society

DT Journal

LA English

AB A novel liposome-based signal amplification system was developed by encapsulating DNA oligonucleotides within antibody-tagged liposomes and subsequently detecting the oligonucleotide with dye-encapsulating liposomes for double signal enhancement. In this sandwich immunoassay, the model analyte, protective antigen protein from *Bacillus anthracis*, was captured by one set of antibodies immobilized in microtiter plate wells and detected using a second antibody conjugated to oligonucleotide-encapsulating liposomes. Bound liposomes were lysed releasing the encapsulated fluorescein-tagged DNA 25-mer probe, which was then permitted to hybridize with its complementary sequence immobilized in a second plate. Finally, the amount of oligonucleotide was detected through the addition of anti-fluorescein antibody tagged dye-encapsulating liposomes. These secondary liposomes allowed for a .apprx.400+ lower LOD than detection of the fluorescein-labeled probe alone. Several aspects were investigated, including the encapsulation of various oligonucleotide concns. within liposomes; oligonucleotide hybridization times and buffers; degree of anti-fluorescein antibody coverage on the liposomes; and immobilized anti-protective antigen antibody concentration. The authors found that the encapsulation efficiency increased with the starting oligonucleotide concentration. As many as 4000 DNA 25-mers were successfully entrapped in the liposome, and minimal leakage was observed over the course of 8 mo. When used in the sandwich immunoassay, a limit of detection of 4.1 ng/mL protective antigen was observed with an upper limit of 5000 ng/mL. Due to the endless combination of DNA oligonucleotide sequences, this assay lends itself perfectly for multiplexing on the order of tens to hundreds of analytes.

IT 184904-19-6

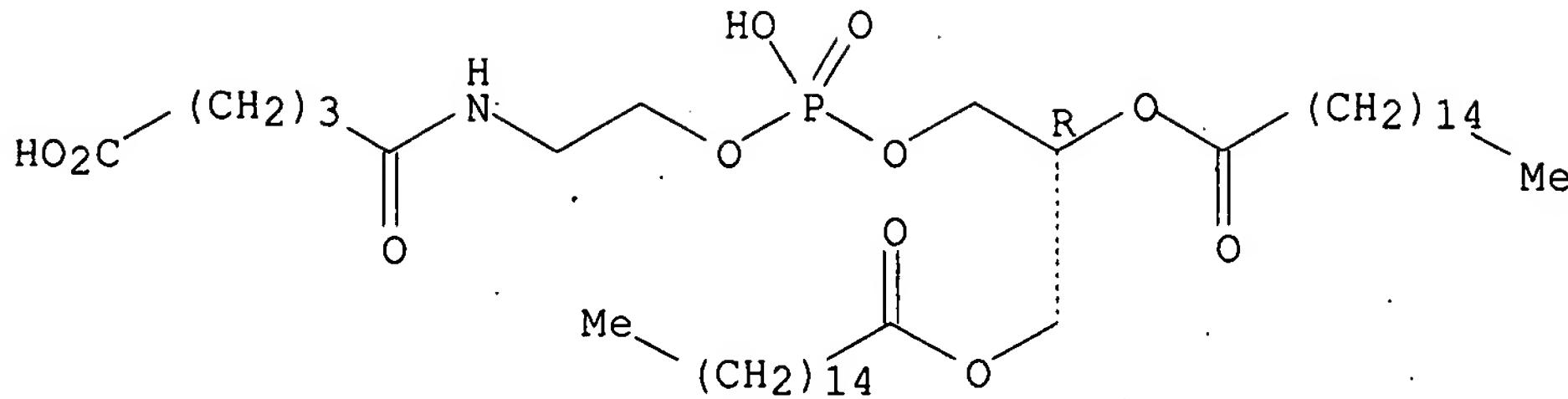
RL: ARU (Analytical role, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(liposomes containing; DNA-oligonucleotide encapsulating antibody-tagged liposomes as secondary signal amplification means)

RN 184904-19-6 CAPLUS

CN 9,11,15-Trioxa-6-aza-10-phosphahentriacontanoic acid, 10-hydroxy-5,16-dioxa-13-[(1-oxohexadecyl)oxy]-, 10-oxide, (13R)- (CA INDEX NAME)

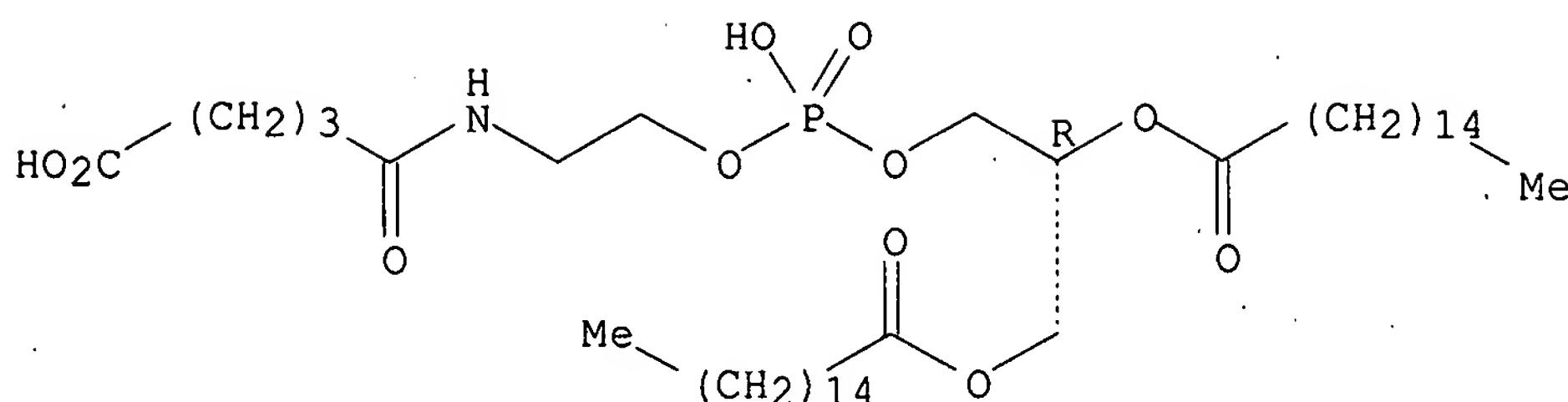
Absolute stereochemistry.



RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 2 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN  
 AN 2006:1199823 CAPLUS  
 DN 146:212403  
 TI In vitro assessment of transferrin-conjugated liposomes as drug delivery systems for inhalation therapy of lung cancer  
 AU Anabousi, Samah; Bakowsky, Udo; Schneider, Marc; Huwer, Hanno; Lehr, Claus-Michael; Ehrhardt, Carsten  
 CS Saarland University, Biopharmaceutics and Pharmaceutical Technology, Saarbruecken, 66123, Germany  
 SO European Journal of Pharmaceutical Sciences (2006), 29(5), 367-374  
 CODEN: EPSCED; ISSN: 0928-0987  
 PB Elsevier B.V.  
 DT Journal  
 LA English  
 AB Most human tumors over-express receptors for growth factors and peptide hormones, which are being increasingly studied as a means to selectively deliver cytotoxic agents. An example being the transferrin receptor (TfR, CD71). Here, the authors studied expression levels and location of TfR in different lung epithelial cell types (i.e., bronchial and alveolar epithelial cells) by flow-cytometry and confocal laser scanning microscopy (CLSM). Furthermore, the authors assessed uptake levels and cytotoxicity of transferrin (Tf)-conjugated liposomes in vitro. TfR was found to be expressed at a significantly higher level in bronchial epithelial cells compared with their alveolar counterparts. Cells of cancerous origin (i.e., A549 cell line) showed a higher TfR expression level than healthy alveolar epithelial type II cells in primary culture. CLSM revealed TfR to be located primarily at the basolateral aspect of cells, with the exception of cells undergoing mitotic proliferation, which also showed TfR at their apical membranes, due to their loss of cell polarity. Higher expression levels of TfR correlated well with enhanced uptake of Tf-liposomes and increased levels of cytotoxicity. Liposome uptake was temperature-dependent and inhibitible by excess free Tf. Tf-conjugated liposomes appear as good candidates for an approach to deliver cytostatic drugs to sites of lung cancer by inhalation.  
 IT 184904-19-6  
 RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (in vitro assessment of transferrin-conjugated liposomes as drug delivery systems for inhalation therapy of lung cancer)  
 RN 184904-19-6 CAPLUS  
 CN 9,11,15-Trioxa-6-aza-10-phosphahentriacontanoic acid, 10-hydroxy-5,16-dioxo-13-[(1-oxohexadecyl)oxy]-, 10-oxide, (13R)- (CA INDEX NAME)

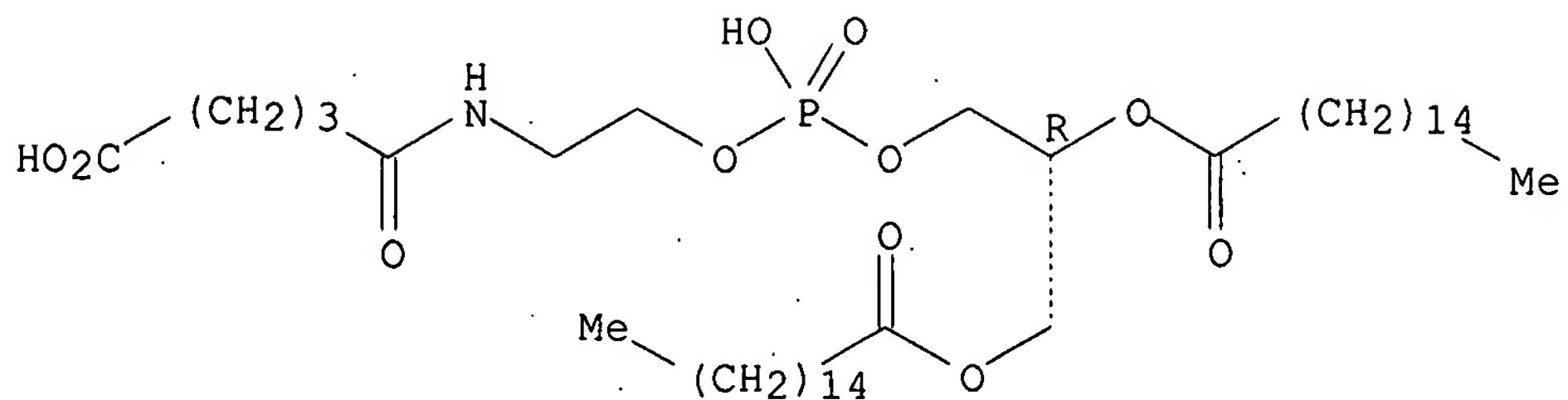
Absolute stereochemistry.



RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN  
 AN 2006:1064013 CAPLUS  
 DN 146:386521  
 TI Effect of PEGylation on the stability of liposomes during nebulisation and in lung surfactant  
 AU Anabousi, Samah; Kleemann, Elke; Bakowsky, Udo; Kissel, Thomas; Schmehl, Thomas; Gessler, Tobias; Seeger, Werner; Lehr, Claus-Michael; Ehrhardt, Carsten  
 CS Department of Biopharmaceutics and Pharmaceutical Technology, Saarland University, Saarbruecken, 66123, Germany  
 SO Journal of Nanoscience and Nanotechnology (2006), 6(9/10), 3010-3016  
 CODEN: JNNOAR; ISSN: 1533-4880  
 PB American Scientific Publishers  
 DT Journal  
 LA English  
 AB Oral inhalation of anticancer drugs or drug delivery system is a novel therapeutic approach in the treatment of lung cancer and requires formulations which are sufficiently stable during nebulization and subsequent interaction with the surfactant lining of the lungs. In this study, we assessed the stability of plain and PEGylated transferrin-conjugated liposomes after nebulization using two different nebulisers (i.e., air-jet and ultrasonic type). Furthermore, the integrity of the liposomal membranes was assessed after incubation in com. lung surfactant solns. (Alveofact). All liposomal formulations showed no significant changes in their size after nebulization, independent of the type of nebuliser or the liposomal formulation, resp. However, PEGylation was of advantage when it came to interactions between liposomes and the surfactant lining of the lungs. PEGylated liposomes were significantly more stable and retained >80% of their drug load over 48 h, which is more than sufficient time for the drug carriers to be taken up by transferrin receptor over-expressing cancer cells in the lung. In conclusion, PEGylated and plain Tf-conjugated liposomes are stable enough to undergo nebulization in the course of an inhalational therapy, but PEG-stabilization results in a higher degree of membrane integrity in lung surfactant.  
 IT 184904-19-6  
 RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (PEGylation effect on stability of liposomes during nebulisation and in lung surfactant)  
 RN 184904-19-6 CAPLUS  
 CN 9,11,15-Trioxa-6-aza-10-phosphahentriacontanoic acid, 10-hydroxy-5,16-dioxo-13-[(1-oxohexadecyl)oxy]-, 10-oxide, (13R)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 4 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN  
AN 2006:976212 CAPLUS  
DN 145:342468  
TI Liposome compositions containing phosphatidylethanolamine dicarboxylate derivatives  
IN Okada, Kazushi; Ibuki, Tadayuki; Kim, Dong Hyeon; Fujisawa, Tadashi  
PA Mebiopharm Co., Ltd., Japan  
SO Jpn. Kokai Tokkyo Koho, 16pp.

CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 2006248978	A	20060921	JP 2005-67469	20050310
	WO 2006099169	A2	20060921	WO 2006-US8650	20060308
	WO 2006099169	A3	20070222		
		W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW		
		RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM		
	US 2006222696	A1	20061005	US 2006-371586	20060308
PRAI	JP 2005-67469	A	20050310		

OS MARPAT 145:342468

AB The invention relates to a drug-containing liposome composition consisting of phospholipids and cholesterol, wherein the phospholipids include phosphatidylethanolamine dicarboxylate derivative 1-12 mol% to the total phospholipids, and does not include non-derivatized phosphatidylethanolamine. The liposome is modified with a ligand having an affinity to target cells through the phosphatidylethanolamine dicarboxylate derivative. The liposome composition enables providing appropriate blood retention property of the active component. For example, liposome composition containing oxaliplatin

as an active component was prepared from oxaliplatin sucrose solution, distearoylphosphatidylcholine, cholesterol, and N-glytaryl-distearoylphosphatidylethanolamine 2:1:0.2. The oxaliplatin-containing liposome was treated with EDC, N-Hydroxysulfosuccinimide, and then transferrin to modify the liposome with transferrin. The blood retention property and antitumor effect of the liposome in tumor-bearing mice were examined

IT 150150-68-8DP, conjugates with transferrin

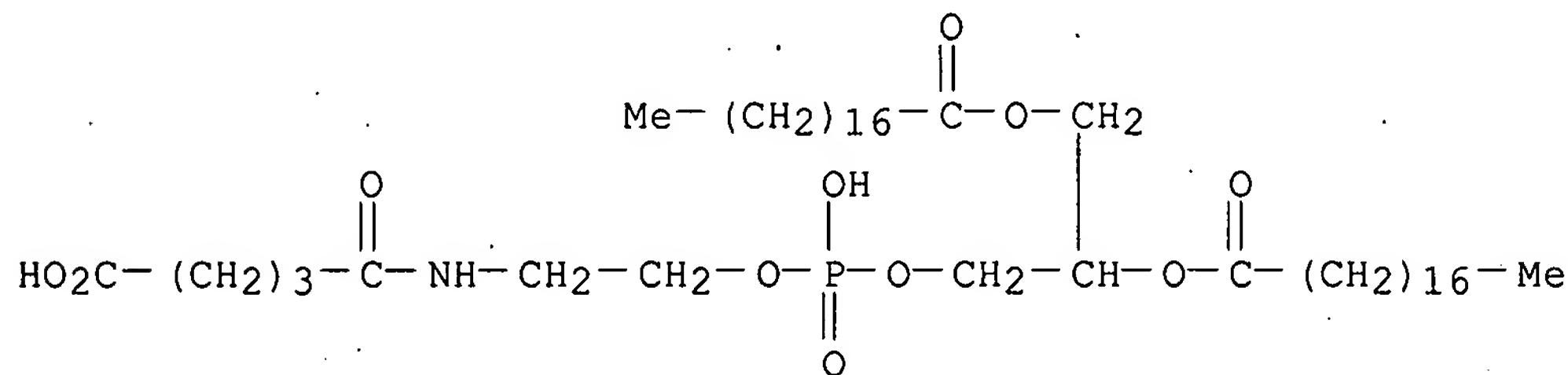
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
(Uses)

(liposome compns. containing phosphatidylethanolamine dicarboxylate derivs.  
conjugated with cell-targeting ligands)

RN 150150-68-8 CAPLUS

CN 9,11,15-Trioxa-6-aza-10-phosphatritriacontanoic acid, 10-hydroxy-5,16-dioxo-13-[(1-oxooctadecyl)oxy]-, 10-oxide (9CI) (CA INDEX NAME)



L13 ANSWER 5 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2005:1001834 CAPLUS

DN 143:282132

TI Multiplex detection probes for microarray assays

IN Murakami, Taku

PA Hitachi Chemical Research Center, Inc., USA; Hitachi Chemical Co., Ltd.

SO PCT Int. Appl., 43 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005084210	A2	20050915	WO 2005-US5955	20050228
	WO 2005084210	A3	20051110		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
	RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	EP 1718662	A2	20061108	EP 2005-723710	20050228
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS			

PRAI US 2004-548635P P 20040227

WO 2005-US5955 W 20050228

AB The present invention comprises detection probes utilizing vesicles or soluble bodies to retain multiple mass tag mols. The detection probes may be used to simultaneously assay a plurality of different biol. samples, each comprising a plurality of analytes, by immobilizing the analytes from each of the samples on a surface incubating the surface with a set of the detection probes, each having mass tag mols. with different masses, removing the unbound detection probe, collecting the first and second mass tag mols. from the bound detection probe, and quantifying the first and second mass tag mols. collected.

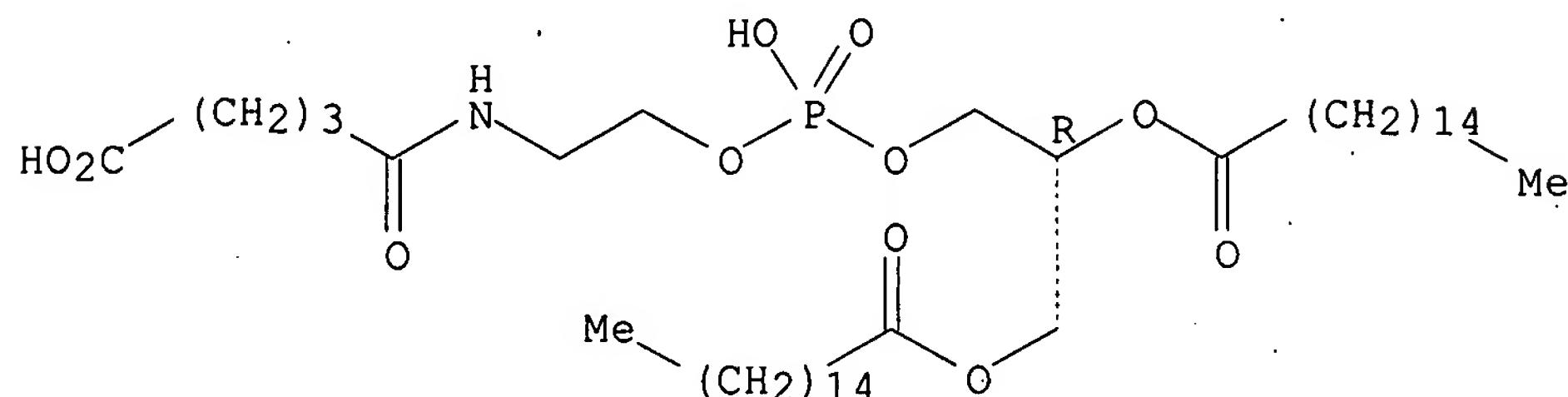
IT 184904-19-6

RL: ARU (Analytical role, unclassified); ANST (Analytical study)  
(multiplex detection probes for microarray assays)

RN 184904-19-6 CAPLUS

CN 9,11,15-Trioxa-6-aza-10-phosphahentriacontanoic acid, 10-hydroxy-5,16-dioxo-13-[(1-oxohexadecyl)oxy]-, 10-oxide, (13R)- (CA INDEX NAME)

## Absolute stereochemistry.



L13 ANSWER 6 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2005:485804 CAPLUS

DN 144:156314

TI Preparation of cationic liposomes modified by polyethylenimine and their application as gene carrier

AU Seo, Dong Hoan; Shin, Byung Cheol; Kim, Moon Suk

CS Nanobiomaterials Laboratory, Korea Research Institute of Chemical Technology, Yuseong, Daejeon, 305-606, S. Korea

SO Polymer (Korea) (2005), 29(3), 277-281

CODEN: POLLDG; ISSN: 0379-153X

## PB Polymer

**DT Journal**

## LA Korean

In this work, we prepared the lipid with polyethylenimine (PEI) to investigate the possibility as effective DNA carrier. Cationic lipid (PEI-DSPE) was synthesized by the reaction of PEI and 1,2-diacyl-sn-glycero-3-phosphoethanolamine (DSPE). The liposomes were prepared by the concentration changes of PEI-DSPE for a mixture of 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), L- $\alpha$ -phosphatidylcholine, hydrogenated (HSPC) and cholesterol (CHOL). Particle size decreased as PEI-DSPE concentration increased. In addition, the charge of liposome surface increased to pos. value according to increasing the relative of PEI-DSPE concentration. The complexation of DNA was confirmed by gel retardation assay and fluorescence measurement. The surface charge of liposome/DNA complexes increased as the liposome concentration or surface charge of liposome increased.

In conclusion, we confirmed that the prepared liposomes have the possibility as a DNA carrier.

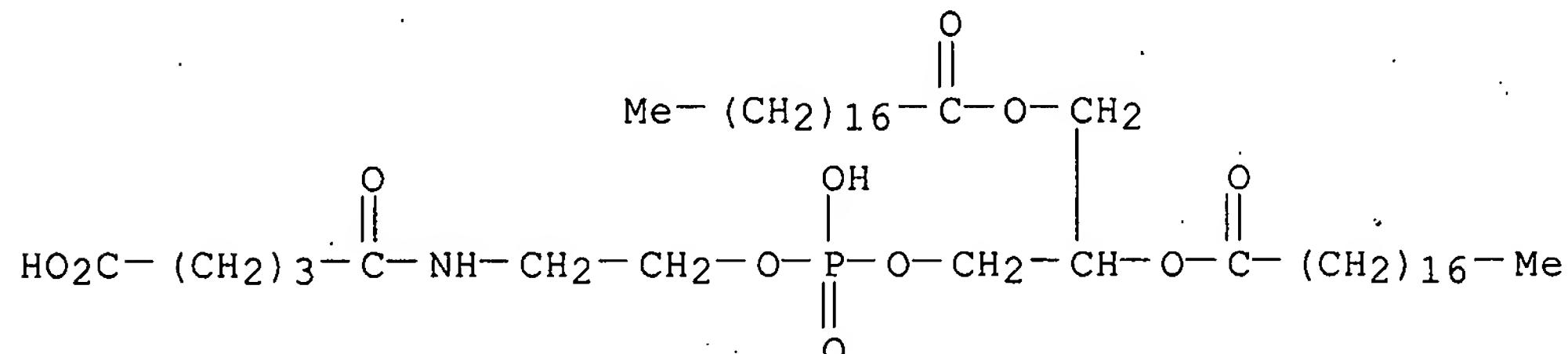
IT 150150-68-8D, reaction products with polyethylenimine

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of cationic liposomes modified by polyethylenimine and their application as gene carrier)

RN 150150-68-8 CAPLUS

CN 9,11,15-Trioxa-6-aza-10-phosphatritriacontanoic acid, 10-hydroxy-5,16-dioxo-13-[(1-oxooctadecyl)oxy]-, 10-oxide (9CI) (CA INDEX NAME)



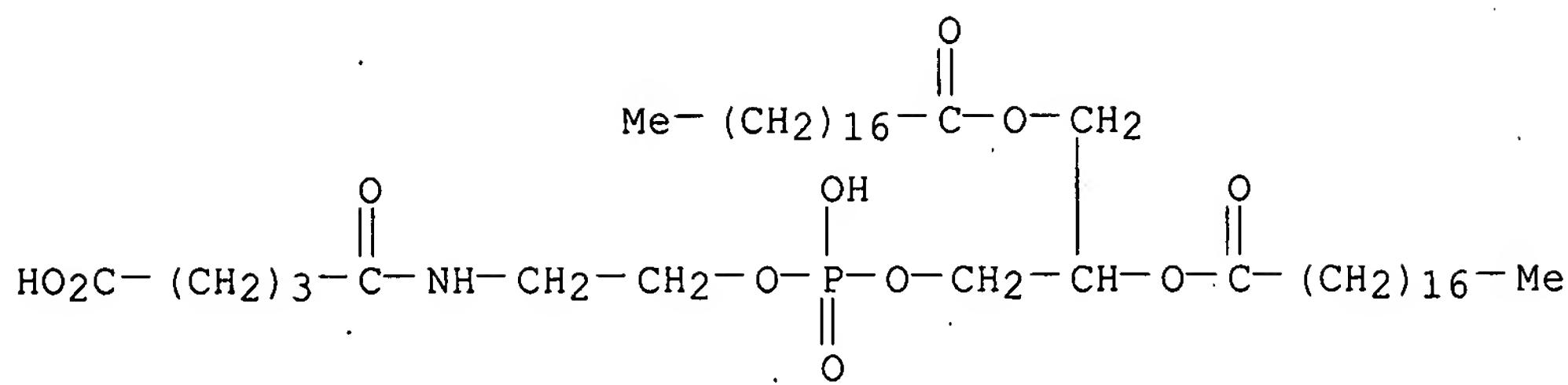
L13 ANSWER 7 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN  
 AN 2004:799592 CAPLUS  
 DN 141:320053  
 TI Phospholipid derivatives for liposome compositions  
 IN Itoh, Chika; Ohhashi, Syunsuke; Kubo, Kazuhiro; Yasukohchi, Tohru;  
     Kikuchi, Hiroshi; Suzuki, Norio; Kurosawa, Miho; Yamauchi, Hitoshi  
 PA NOF Corporation, Japan; Daiichi Pharmaceutical Co. Ltd.  
 SO PCT Int. Appl., 39 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA Japanese  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004083219	A1	20040930	WO 2004-JP3789	20040319
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRAI	US 2007031481	A1	20070208	US 2006-549630	20060817
	JP 2003-77242	A	20030320		
	WO 2004-JP3789	W	20040319		
AB	A phospholipid derivative represented by the formula $R_1COCH_2CH(OCR_2)CH_2OP(OX)O_2CH_2CH_2NHCO(CH_2)_a(CO)bO(A_1O)_m(A_2O)_n(A_3O)_qR_3$ (R <sub>1</sub> CO, R <sub>2</sub> CO = acyl; R <sub>3</sub> = H, hydrocarbon; a = 0-4; b = 0-1, provided that when a is 0, then b is 0; X = H, alkali metal, ammonium, organic ammonium; A <sub>1</sub> O, A <sub>2</sub> O, and A <sub>3</sub> O = oxyalkylene, provided that the proportion of oxyethylene in A <sub>1</sub> O and A <sub>3</sub> O is 0.5 or higher by weight; and m, n, and q each indicates the average number of moles added, provided that 5 ≤ m ≤ 600, 1 ≤ n ≤ 45, 0 ≤ q ≤ 200, 10 ≤ m + n + q ≤ 600, 0.04 ≤ n/(m + n + q), and q/(m + n + q) ≤ 0.8). The derivative, on the surface of a liposome, is inhibited from spreading its polyalkylene oxide structure and thus serves to increase the amount of the hydrated layer on the surface and thereby heighten the stability of the liposome. A phospholipid compound monomethyl polyoxypropylene-polyoxyethylenesuccinyl distearoylphosphatidylethanolamine was prepared. The phospholipid 1.04 mM was mixed with hydrogenated soybean phosphatidylcholine (HSPC) 11.28 cholesterol 7.68 mM, and doxorubicin solution q.s. to form a liposome with an average particle size of 95 nm.				
IT	766509-41-5P, Monomethyl polyoxypropylene-polyoxyethylene glutaryl distearoylphosphatidylethanolamine RL: COS (Cosmetic use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (phospholipid derivs. for liposome compns.)				
RN	766509-41-5 CAPLUS				
CN	Oxirane, methyl-, polymer with oxirane, mono[10-hydroxy-10-oxido-5,16-dioxo-13-[(1-oxooctadecyl)oxy]-9,11,15-trioxa-6-aza-10-phosphatritriacanthanoate], methyl ether (9CI) (CA INDEX NAME)				

CM 1

CRN 150150-68-8

CMF C46 H88 N O11 P



CM 2

CRN 67-56-1

CMF C H4 O

H<sub>3</sub>C-OH

CM 3

CRN 9003-11-6

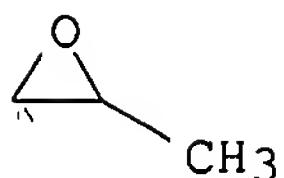
CMF (C<sub>3</sub> H<sub>6</sub> O . C<sub>2</sub> H<sub>4</sub> O)x

CCI PMS

CM 4

CRN 75-56-9

CMF C<sub>3</sub> H<sub>6</sub> O



CM 5

CRN 75-21-8

CMF C<sub>2</sub> H<sub>4</sub> O



L13 ANSWER 8 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2004:633410 CAPLUS

DN 141:179562

TI Multivalent constructs for therapeutic and diagnostic applications

IN Arbogast, Christophe; Bussat, Philippe; Dransfield, Daniel T.; Fan, Hong; Linder, Karen; Marinelli, Edmund R.; Nanjappan, Palaniappa; Nunn, Adrian; Pillai, Radhakrishna; Pochon, Sybille; Ramalingam, Kondareddiar; Sato, Aaron; Shrivastava, Ajay; Song, Bo; Swenson, Rolf E.; Von Wronski, Mathew A.; Walker, Sharon Michele

PA Bracco International B. V., Neth.; Dyax Corporation

SO PCT Int. Appl., 320 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004064595	A2	20040805	WO 2003-US28838	20030911
	WO 2004064595	A3	20050331		
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	US 2004018974	A1	20040129	US 2003-379287	20030303
	US 7211240	B2	20070501		
	CA 2512780	A1	20040805	CA 2003-2512780	20030911
	AU 2003276884	A1	20040813	AU 2003-276884	20030911
	EP 1587523	A2	20051026	EP 2003-815479	20030911
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			

PRAI US 2003-440201P P 20030115  
US 2003-379287 A 20030303  
US 2002-360821P P 20020301  
WO 2003-US28838 W 20030911

AB The invention features multivalent constructs using small targeting moieties which bind to different sites of the same target allowing for improved localization to the desired target and providing improved means for detecting, imaging and/or treating the target site. These targeting constructs may be linked or conjugated to a detectable label and/or a therapeutic agent and used to deliver the detectable label and/or therapeutic agent to the target of interest. The target may be a receptor involved in angiogenesis, hyperproliferative disorders or wound healing. Among examples provided are human carcinoma cell growth inhibition by an antiangiogenic heterodimeric peptide binding to VEGF receptor 2 (KDR), and ultrasound imaging using microbubbles derivatized with a KDR-binding heterodimer.

IT 123689-62-3D, derivs.

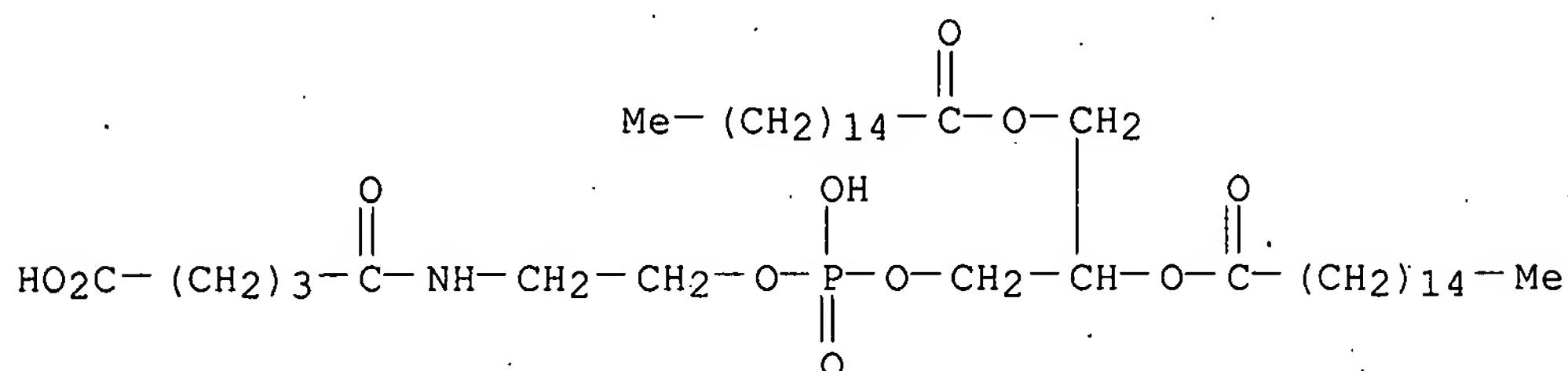
RL: DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study);

USES (Uses)

(multivalent constructs for therapeutic and diagnostic applications)

RN 123689-62-3 CAPLUS

CN 9,11,15-Trioxa-6-aza-10-phosphahentriacontanoic acid, 10-hydroxy-5,16-dioxo-13-[(1-oxohexadecyl)oxy]-, 10-oxide (9CI) (CA INDEX NAME)



L13 ANSWER 9 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2004:610131 CAPLUS

DN 141:162358

TI Conjugate for retention in blood and cancer tissue-specific drug delivery  
IN Maeda, Atsushi; Takagi, Akira; Saito, Katsumi; Yamashita, Noboru;

PA Yoshioka, Tatsunobu  
 SO Yamanouchi Pharmaceutical Co., Ltd., Japan  
 PCT Int. Appl., 77 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA Japanese  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004063216	A1	20040729	WO 2004-JP104	20040109
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ				
	US 2005054026	A1	20050310	US 2004-754341	20040109
	US 7169892	B2	20070130		
	EP 1591450	A1	20051102	EP 2004-701116	20040109
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRAI US 2003-439560P P 20030110  
WO 2004-JP104 W 20040109

AB Disclosed are a conjugate of a lipid, a peptide serving as the substrate of an enzyme secreted from cells of mammals including humans and a water-soluble polymer, which is usable as a colloidal carrier in a tissue-specific drug delivery system, etc.; a process for producing the conjugate; a peptide/water-soluble polymer conjugate optionally having a protective group which is useful as an intermediate of the conjugate; a colloidal carrier comprising the conjugate; and a tissue-specific drug delivery system using the colloidal carrier. Thus, distearoylphosphatidylethanolamine-glutaryl-Gly-Pro-Gln-Gly-Ile-Ala-Gly-Trp-Gly-amidopropyl polyoxyethylene Me ether was prepared for making liposome composition. The blood retention property and cancer-targeting property of the liposome was examined in mice.

IT 150150-68-8P

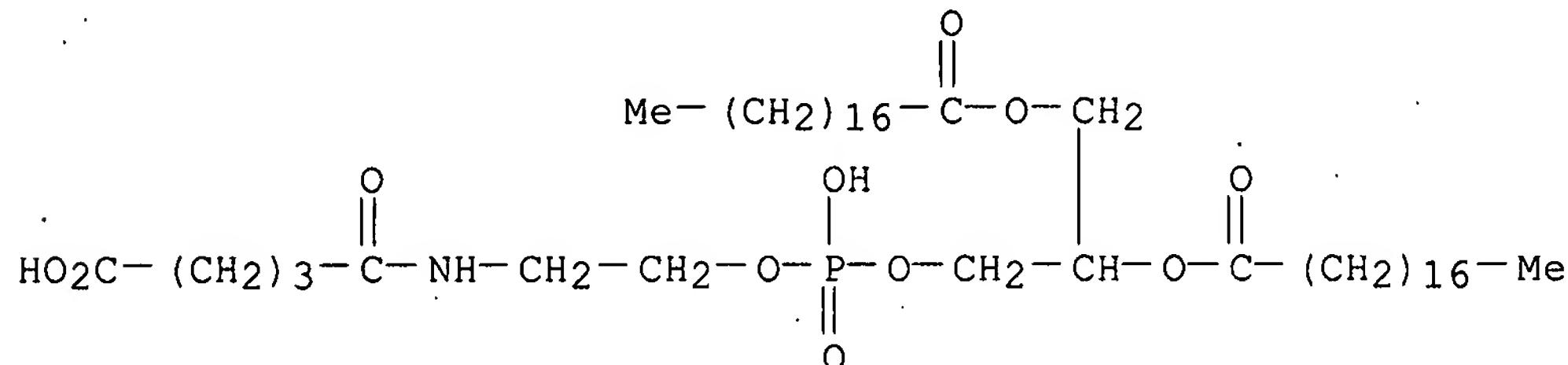
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation of conjugate for retention in blood and cancer tissue-specific drug delivery containing lipids, water-soluble polymers, and peptides

serving

as substrates of specified enzymes)

RN 150150-68-8 CAPLUS

CN 9,11,15-Trioxa-6-aza-10-phosphatritriacontanoic acid, 10-hydroxy-5,16-dioxo-13-[(1-oxooctadecyl)oxy]-, 10-oxide (9CI) (CA INDEX NAME)



L13 ANSWER 10 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2004:589555 CAPLUS

DN 141:142211

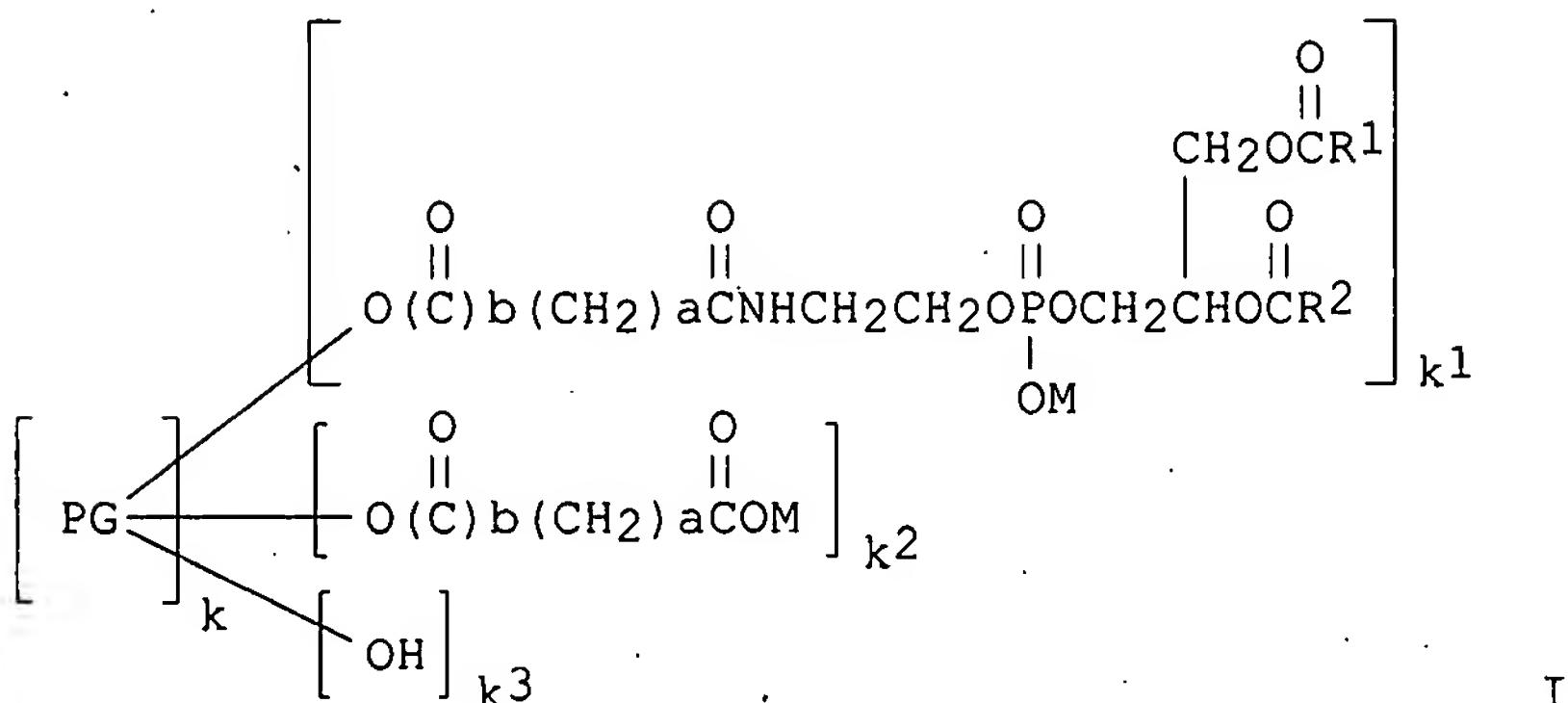
TI Phospholipid derivatives used for surfactants, solubilizers, dispersants in cosmetics and lipid membranes and their preparation

IN Kubo, Kazuhiro; Itoh, Chika; Ohhashi, Syunsuke; Yasukohchi, Tohru; Ohkawa, Yusuke; Kikuchi, Hiroshi; Suzuki, Norio; Kurosawa, Miho; Yamauchi, Hitoshi

PA NOF Corporation, Japan; Daiichi Pharmaceutical Co., Ltd.  
 SO PCT Int. Appl., 52 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA Japanese  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004060899	A1	20040722	WO 2003-JP15969	20031212
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2513144	A1	20040722	CA 2003-2513144	20031212
	AU 2003289070	A1	20040729	AU 2003-289070	20031212
	EP 1591447	A1	20051102	EP 2003-778894	20031212
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	CN 1735624	A	20060215	CN 2003-80108368	20031212
	US 2006210618	A1	20060921	US 2005-541309	20050705
PRAI	JP 2003-330	A	20030106		
	WO 2003-JP15969	W	20031212		

GI



AB The phospholipid derivs. I ( $[PG]k$  = residue of a polyglycerol having d.p.  $k$ ;  $k = 2-50$ ;  $R_1CO$ ,  $R_2CO = C8-22$  acyl;  $a = 0-5$ ;  $b = 0-1$ ;  $M = H$ , alkali metal, ammonium or organic ammonium; and  $k_1$ ,  $k_2$ ,  $k_3$  = nos. satisfying the relationships:  $1 \leq k_1 \leq (k + 2)/2$ ,  $0 \leq k_2$ , and  $k_1 + k_2 + k_3 = k + 2$ ). The derivs. are highly safe for the living body and can be favorably utilized in drug delivery systems such as liposome.

IT 725724-24-3P 725724-25-4P 725724-26-5P  
 725724-32-3P

RL: BUU (Biological use, unclassified); COS (Cosmetic use); IMF (Industrial manufacture); TEM (Technical or engineered material use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of phospholipid derivs. used for surfactants, solubilizers, dispersants in cosmetics and lipid membranes)

RN 725724-24-3 CAPLUS

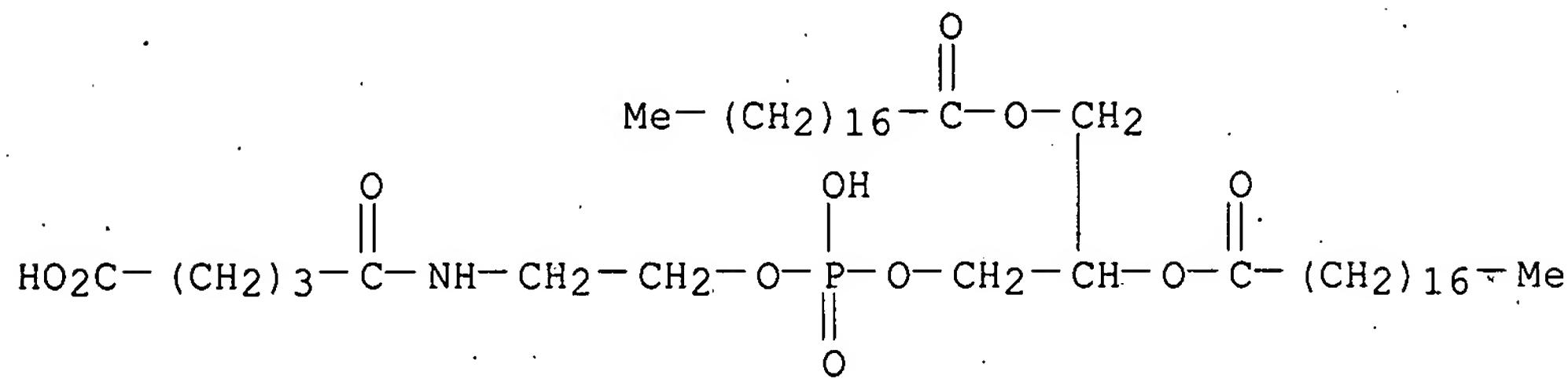
CN 9,11,15-Trioxa-6-aza-10-phosphatritriacontanoic acid, 10-hydroxy-5,16-

dioxo-13-[(1-oxooctadecyl)oxy]-, 10-oxide, ester with hexaglycerol (9CI)  
(CA INDEX NAME)

CM 1

CRN 150150-68-8

CMF C46 H88 N O11 P



CM 2

CRN 36675-34-0

CMF C18 H38 O13

CCI IDS, MAN

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

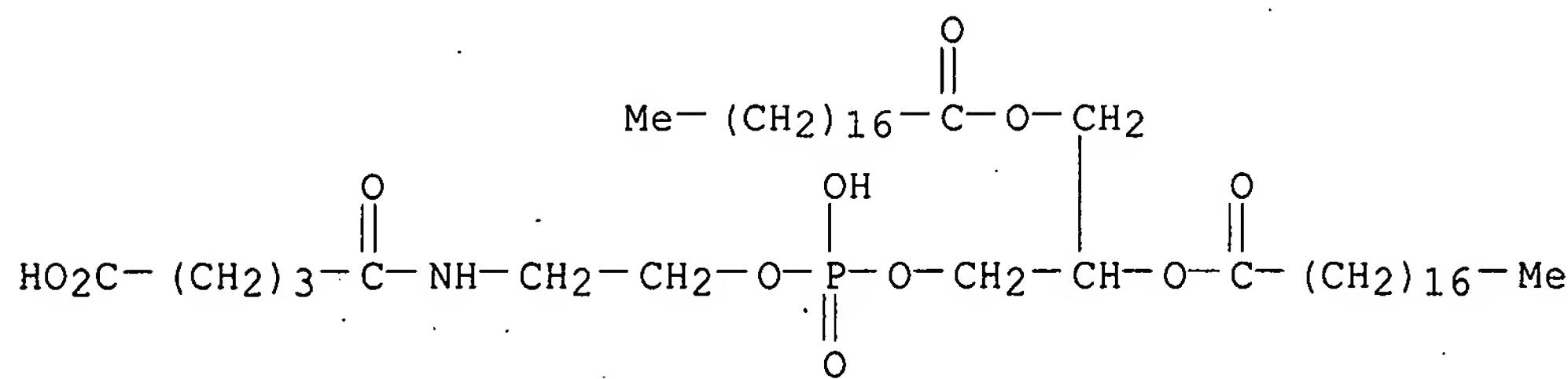
RN 725724-25-4 CAPLUS

CN 9,11,15-Trioxa-6-aza-10-phosphatritriacontanoic acid, 10-hydroxy-5,16-dioxo-13-[(1-oxooctadecyl)oxy]-, 10-oxide, ester with octaglycerol (9CI)  
(CA INDEX NAME)

CM 1

CRN 150150-68-8

CMF C46 H88 N O11 P



CM 2

CRN 70103-30-9

CMF C24 H50 O17

CCI IDS, MAN

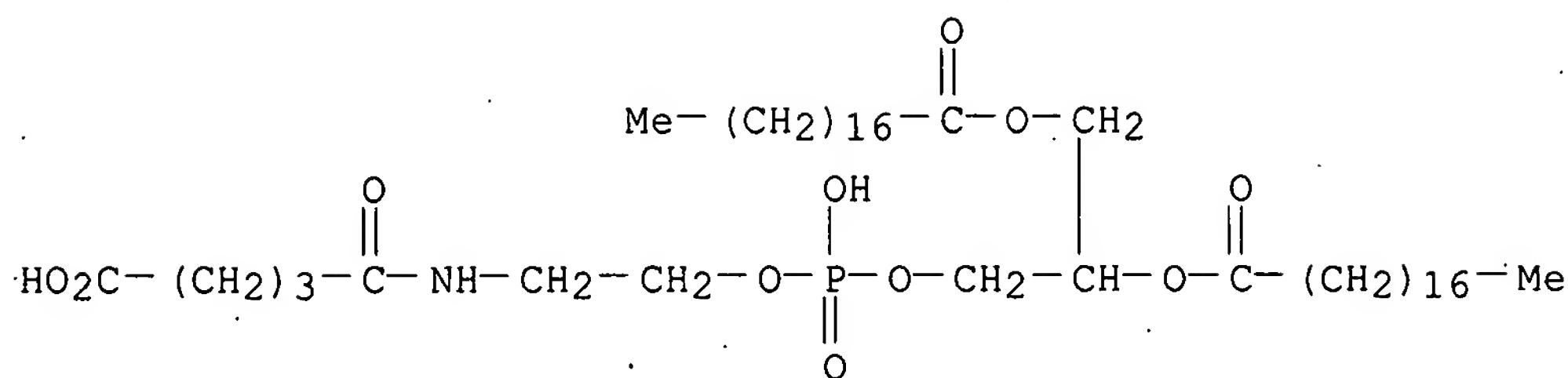
\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

RN 725724-26-5 CAPLUS

CN 9,11,15-Trioxa-6-aza-10-phosphatritriacontanoic acid, 10-hydroxy-5,16-dioxo-13-[(1-oxooctadecyl)oxy]-, 10-oxide, ester with decaglycerol (9CI)  
(CA INDEX NAME)

CM 1

CRN 150150-68-8  
CMF C46 H88 N O11 P



CM 2

CRN 9041-07-0  
CMF C30 H62 O21  
CCI IDS, MAN

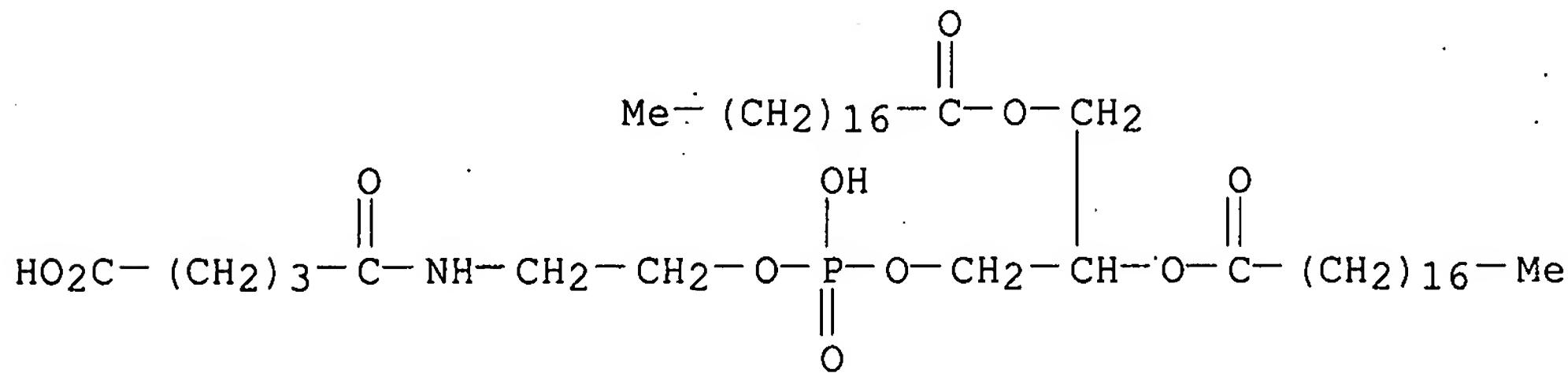
\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

RN 725724-32-3 CAPLUS

CN Butanedioic acid, ester with octaglycerol 10-hydroxy-5,16-dioxo-13-[(1-oxooctadecyl)oxy]-9,11,15-trioxa-6-aza-10-phosphatritriacontanoate 10-oxide (8:1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 150150-68-8  
CMF C46 H88 N O11 P



CM 2

CRN 70103-30-9  
CMF C24 H50 O17  
CCI IDS, MAN

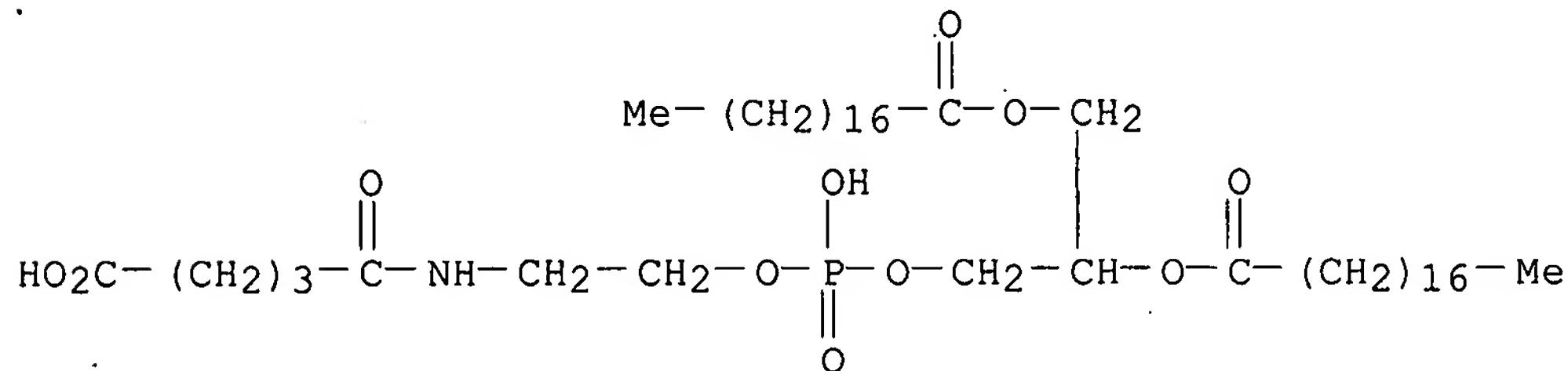
\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

CM 3

CRN 110-15-6  
CMF C4 H6 O4

$\text{HO}_2\text{C} - \text{CH}_2 - \text{CH}_2 - \text{CO}_2\text{H}$

IT 150150-68-8P  
 RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation of phospholipid derivs. used for surfactants, solubilizers, dispersants in cosmetics and lipid membranes)  
 RN 150150-68-8 CAPLUS  
 CN 9,11,15-Trioxa-6-aza-10-phosphatritriacontanoic acid, 10-hydroxy-5,16-dioxo-13-[(1-oxooctadecyl)oxy]-, 10-oxide (9CI) (CA INDEX NAME)



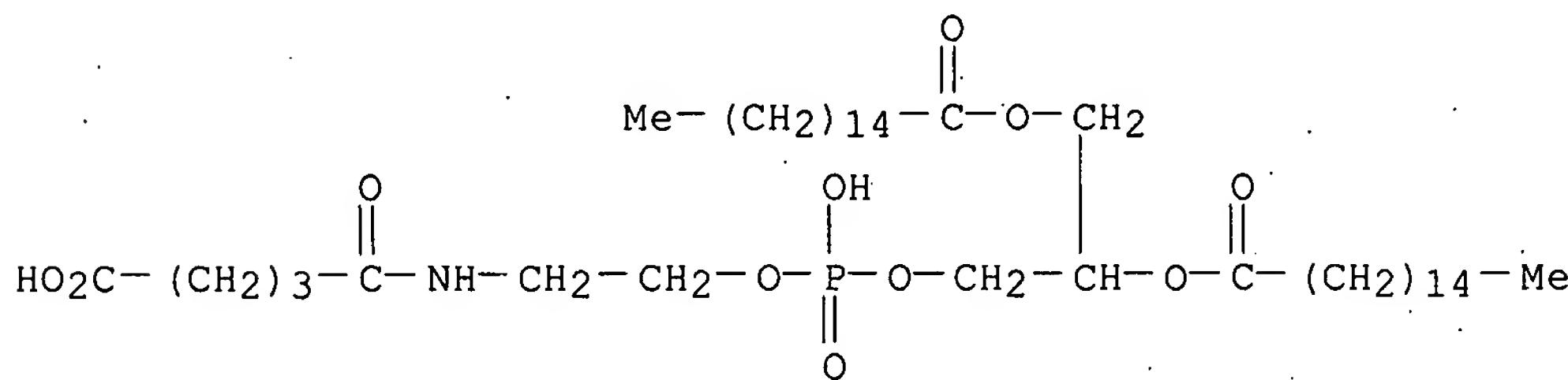
L13 ANSWER 11 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN  
 AN 2003:818316 CAPLUS  
 DN 139:328319  
 TI Multivalent constructs for therapeutic and diagnostic applications  
 IN Arbogast, Christophe; Bussat, Philippe; Dransfield, Daniel T.; Fan, Hang; Linder, Karen E.; Marinelli, Edmund R.; Nanjappan, Palaniappa; Nunn, Adrian; Pillai, Radhakrishna; Pochon, Sybille; Ramalingam, Kondareddiar; Sato, Aaron; Shrivastava, Ajay; Song, Bo; Swenson, Rolf E.; Von Wronski, Mathew A.; Walker, Sharon Michele  
 PA Bracco International BV, Neth.; Dyax Corp.  
 SO PCT Int. Appl., 278 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003084574	A1	20031016	WO 2003-US6656	20030303
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2477935	A1	20031016	CA 2003-2477935	20030303
	AU 2003228276	A1	20031020	AU 2003-228276	20030303
	EP 1482987	A1	20041208	EP 2003-726024	20030303
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	JP 2005519980	T	20050707	JP 2003-581813	20030303
PRAI	US 2002-360821P	P	20020301		
	US 2003-440201P	P	20030115		
	WO 2003-US6656	W	20030303		

AB The invention features multivalent constructs using small targeting moieties which bind to different sites of the same target allowing for improved localization to the desired target and providing improved means for detecting, imaging and/or treating the target site. These targeting constructs may be linked or conjugated to a detectable label and/or a

therapeutic agent and used to deliver the detectable label and/or therapeutic agent to the target of interest. The target may be a receptor involved in angiogenesis, hyperproliferative disorders or wound healing. Among examples provided are human carcinoma cell growth inhibition by an antiangiogenic heterodimeric peptide binding to VEGF receptor 2 (KDR), and ultrasound imaging using microbubbles derivatized with a KDR-binding heterodimer.

IT 123689-62-3D, derivs.  
 RL: DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study);  
 USES (Uses)  
 (multivalent constructs for therapeutic and diagnostic applications)  
 RN 123689-62-3 CAPLUS  
 CN 9,11,15-Trioxa-6-aza-10-phosphahentriacontanoic acid, 10-hydroxy-5,16-dioxo-13-[(1-oxohexadecyl)oxy]-, 10-oxide (9CI) (CA INDEX NAME)



RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 12 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN  
 AN 2003:796716 CAPLUS  
 DN 139:296564  
 TI Phospholipid derivatives for cosmetic and pharmaceutical uses  
 IN Itoh, Chika; Kubo, Kazuhiko; Ohhashi, Syunsuke; Yasukohchi, Tohru; Kikuchi, Hiroshi; Suzuki, Norio; Kurosawa, Miho; Yamauchi, Hitoshi  
 PA NOF Corporation, Japan; Daiichi Pharmaceutical Co., Ltd.  
 SO PCT Int. Appl., 47 pp.

CODEN: PIXXD2

DT Patent.  
 LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003082882	A1	20031009	WO 2003-JP3966	20030328
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2003220917	A1	20031013	AU 2003-220917	20030328
	EP 1498420	A1	20050119	EP 2003-715589	20030328
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	US 2005220856	A1	20051006	US 2005-508704	20050525
PRAI	JP 2002-93694	A	20020329		
	WO 2003-JP3966	W	20030328		
AB	Disclosed is a phospholipid derivative which is highly safe for the living body and is suitable for use in solubilizing or dispersing a physiol.				

active substance, etc. or in the field of drug delivery systems, e.g., a liposome, or cosmetics. The phospholipids comprise polyalkylene oxide groups. For example, polyoxyethylene pentaerythritol ether glutaryl-mono(distearoylphosphatidylethanolamine succinate) was prepared and used as a solubilizer in formulating lotions.

IT 609844-35-1P

RL: COS (Cosmetic use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of phospholipid derivs. for cosmetic and pharmaceutical uses)

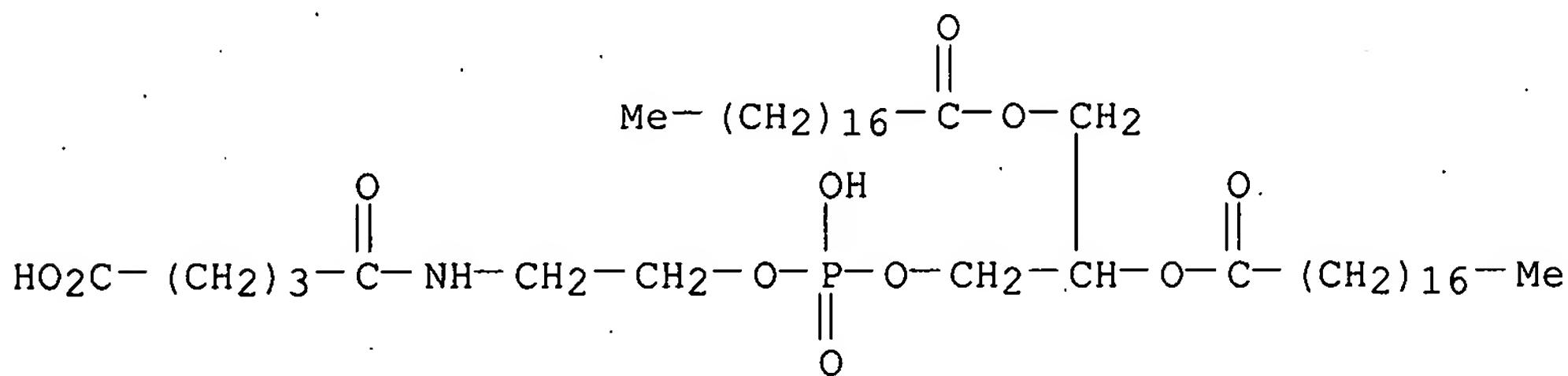
RN 609844-35-1 CAPLUS

CN Poly(oxy-1,2-ethanediyl),  $\alpha$ -hydro- $\omega$ -hydroxy-, ether with  
oxybis[propanol] (4:1), mono(10-hydroxy-5,16-dioxo-13-[(1-  
oxooctadecyl)oxy]-9,11,15-trioxa-6-aza-10-phosphatritriacontanoate  
10-oxide) (9CI) (CA INDEX NAME)

CM 1

CRN 150150-68-8

CMF C46 H88 N O11 P



CM 2

CRN 59113-36-9

CMF C6 H14 O5

CCI IDS, MAN

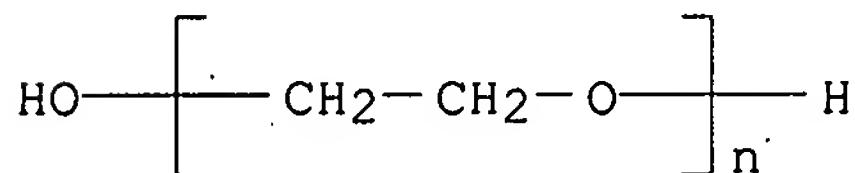
\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

CM 3

CRN 25322-68-3

CMF (C<sub>2</sub> H<sub>4</sub> O)<sub>n</sub> H<sub>2</sub> O

CCI PMS



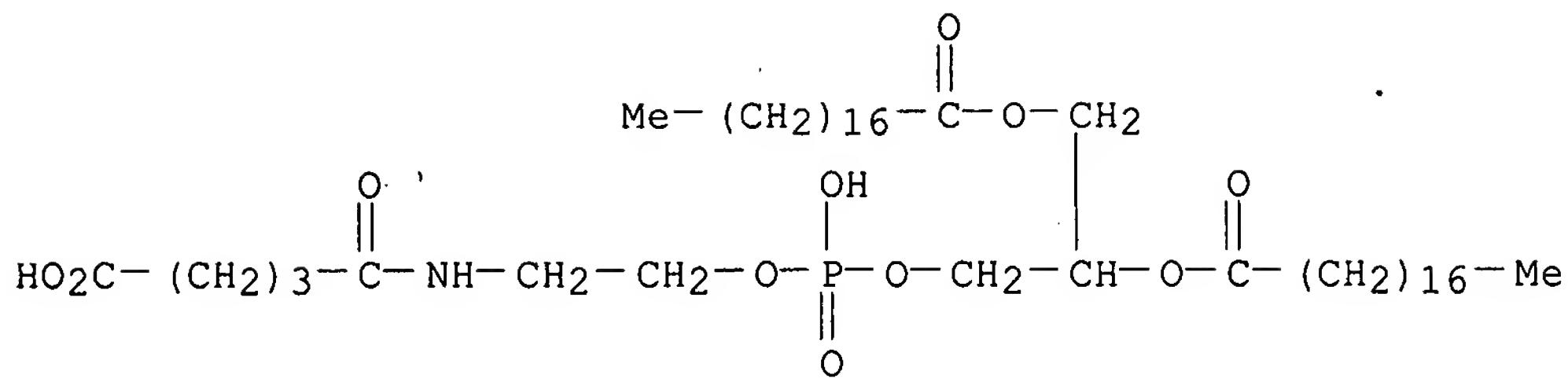
IT 150150-68-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)

(preparation of phospholipid derivs. for cosmetic and pharmaceutical uses)

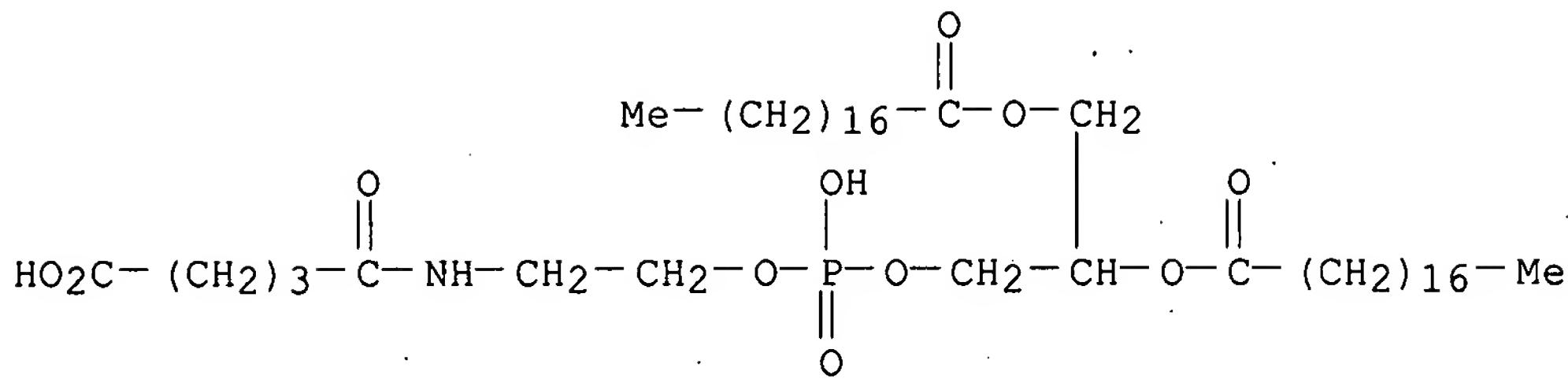
RN 150150-68-8 CAPLUS

CN 9,11,15-Trioxa-6-aza-10-phosphatritriacontanoic acid, 10-hydroxy-5,16-  
dioxo-13-[(1-oxooctadecyl)oxy]-, 10-oxide (9CI) (CA INDEX NAME)



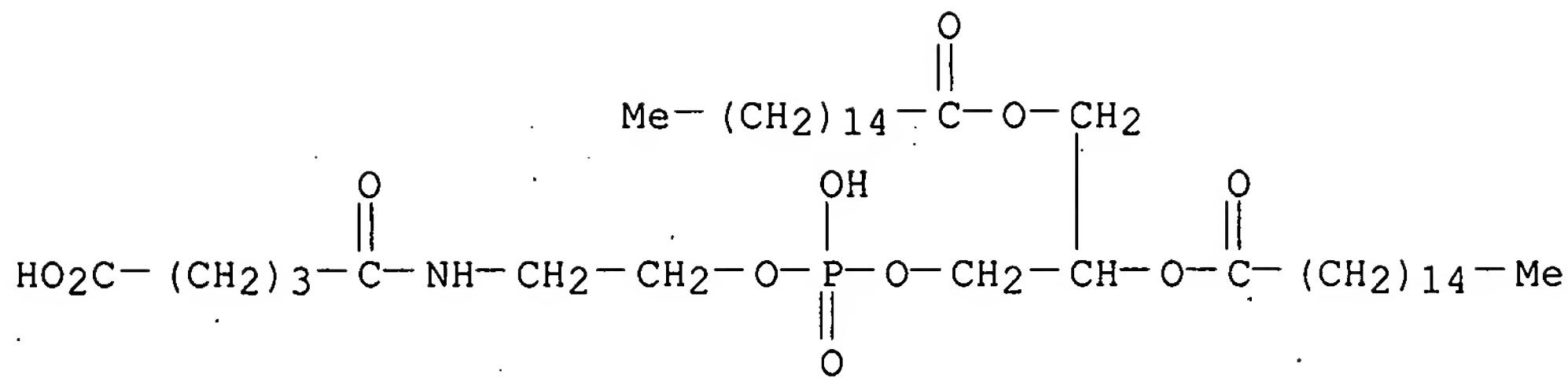
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 13 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN  
AN 2001:549174 CAPLUS  
DN 136:107385  
TI Liposomes bearing polyethyleneglycol-coupled transferrin with intracellular targeting property to the solid tumors in vivo  
AU Ishida, Osamu; Maruyama, Kazuo; Tanahashi, Hiroyuki; Iwatsuru, Motoharu; Sasaki, Katsunori; Eriguchi, Masazumi; Yanagie, Hironobu  
CS Faculty of Pharmaceutical Sciences, Teikyo University, Kanagawa, 199-0195, Japan  
SO Pharmaceutical Research (2001), 18(7), 1042-1048  
CODEN: PHREEB; ISSN: 0724-8741  
PB Kluwer Academic/Plenum Publishers  
DT Journal  
LA English  
AB The purpose of this study was to determine the usefulness of transferrin (TF)-pendant-type polyethyleneglycol (PEG)-liposomes (TF-PEG-liposomes), in which TF was covalently linked to the distal terminal of PEG chains on the external surface of PEG-liposomes as a carrier for in vivo cytoplasmic targeting to tumor cells. Small unilamellar TF-PEG-liposomes (100-140 nm in diameter) were prepared from DSPC, CH, DSPE-PEG, and DSPE-PEG-COOH (2:1:0.11:0.021, molar ratio), and were conjugated to TF via the carboxyl residue of DSPE-PEG-COOH. The intracellular targeting ability of TF-PEG-liposomes to tumor cells was examined in vitro and in Colon 26 tumor-bearing mice. TF-PEG-liposomes, bearing approx. 25 TF mols. per liposome, readily bound to mouse Colon 26 cells in vitro and were internalized by receptor-mediated endocytosis. TF-PEG-liposomes showed a prolonged residence time in the circulation and low RES uptake in Colon 26 tumor-bearing mice, resulting in enhanced extravasation of the liposomes into the solid tumor tissue. Electron microscopic studies in Colon 26 tumor-bearing mice revealed that the extravasated TF-PEG-liposomes were internalized into tumor cells by receptor-mediated endocytosis. TF-PEG-liposomes had the capabilities of specific receptor binding and receptor-mediated endocytosis to target cells after extravasation into solid tumors in vivo. Such liposomes should be useful for in vivo cytoplasmic targeting of chemotherapeutic agents or plasmid DNAs to target cells.  
IT 150150-68-8P  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(liposomes bearing PEG-coupled transferrin with intracellular targeting property to solid tumors in vivo)  
RN 150150-68-8 CAPLUS  
CN 9,11,15-Trioxa-6-aza-10-phosphatritriacontanoic acid, 10-hydroxy-5,16-dioxo-13-[(1-oxooctadecyl)oxy]-, 10-oxide (9CI) (CA INDEX NAME)



RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 14 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN  
 AN 2001:470561 CAPLUS  
 DN 136:221629  
 TI Synthesis of RGD containing peptides. Comparative study of their incorporation to the surface of 5-fluorouridine loaded liposomes  
 AU Massaguer, A.; Haro, I.; Alsina, M. A.; Reig, F.  
 CS Department of Peptide and Protein Chemistry, IIQAB-CSIC, Barcelona, 08034, Spain  
 SO Journal of Liposome Research (2001), 11(1), 103-113  
 CODEN: JLREE7; ISSN: 0898-2104  
 PB Marcel Dekker, Inc.  
 DT Journal  
 LA English  
 AB The synthesis on solid phase of a peptide sequence (GGRGRS) related to an integrin adhesion site as well as the preparation of some hydrophobic derivs. is described. The incorporation of these peptides to the surface of liposomes was carried out either through the NGPE (N-glutaryl dipalmitoyl phosphatidylcholine) carboxyl-group or mixing hydrophobic peptide derivs. with lipids since the beginning of the process. The influence of these factors on the entrapment yield of 5-FUR (5-fluorouridine) was determined. Best results, calculated as percentage of drug encapsulation, were obtained when the peptide was linked to preformed liposomes via an NGPE-amide bond. On the contrary, the presence of these hydrophobic peptides on the bilayers decreases the overall yield of encapsulation of 5-FUR. Nevertheless, considering drug/lipid relationship and scaling-up requirements it seems that the use of myristoyl peptide derivative should be the procedure of choice. Physicochem. studies carried out with the peptides indicated that the presence of hydrophobic moieties linked to the parent peptide increases the tendency to self aggregation, as detected through fluorescence studies using DPH (1,6-di-Ph hexatriene) as marker, reducing in this way the efficiency of incorporation of hydrophobic peptides to the surface of liposomes.  
 IT 123689-62-3P  
 RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of RGD-containing peptides and their incorporation to surface of 5-fluoruridine-loaded liposomes)  
 RN 123689-62-3 CAPLUS  
 CN 9,11,15-Trioxa-6-aza-10-phosphahentriacontanoic acid, 10-hydroxy-5,16-dioxo-13-[(1-oxohexadecyl)oxy]-, 10-oxide (9CI) (CA INDEX NAME)



RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 15 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2000:865087 CAPLUS

DN 134:21485

TI Liposome vector complexes for gene therapy

IN Bruesselbach, Sabine; Mueller, Kristina; Fahr, Alfred

PA Aventis Pharma Deutschland G.m.b.H., Germany

SO Ger. Offen., 14 pp.

CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 19925143	A1	20001207	DE 1999-19925143	19990602
	CA 2375854	A1	20001214	CA 2000-2375854	20000523
	WO 2000074646	A2	20001214	WO 2000-EP4678	20000523
	WO 2000074646	A3	20010809		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BE, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	EP 1187929	A2	20020320	EP 2000-929548	20000523
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
	JP 2003501373	T	20030114	JP 2001-501183	20000523
PRAI	DE 1999-19925143	A	19990602		
	WO 2000-EP4678	W	20000523		

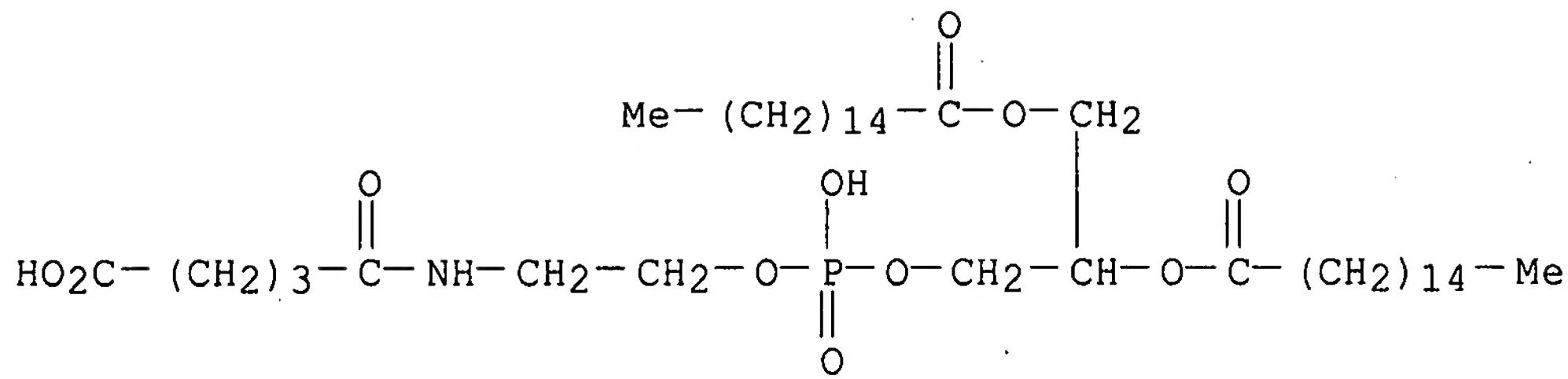
AB The invention refers to a new liposome carrier complex, containing the following components: (A) a nucleic acid sequence of arbitrary length; (B) a cationic carrier, (C) lipids and phospholipids and (D) optionally a ligand, and (E) optionally a functional sequence from the subunit HA-2 hemagglutinins of the influenza virus. Human umbilical cord endothelial cells, which were incubated with the liposomes, showed a clear expression of cDNA.

IT 123689-62-3P

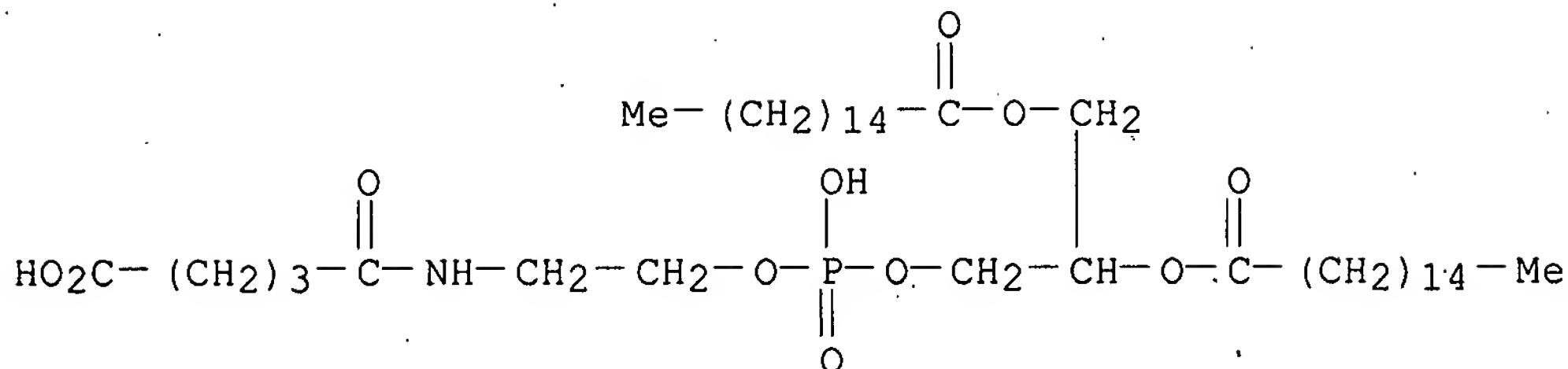
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(liposome vector complexes for gene therapy)

RN 123689-62-3 CAPLUS

CN 9,11,15-Trioxa-6-aza-10-phosphatetracontanoic acid, 10-hydroxy-5,16-dioxa-13-[(1-oxohexadecyl)oxy]-, 10-oxide (9CI) (CA INDEX NAME)



L13 ANSWER 16 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN  
 AN 1997:601246 CAPLUS  
 DN 127:298616  
 TI Enhancement of the in vivo circulation lifetime of L- $\alpha$ -distearoylphosphatidylcholine liposomes: importance of liposomal aggregation versus complement opsonization  
 AU Ahl, Patrick L.; Bhatia, Suresh K.; Meers, Paul; Roberts, Patricia; Stevens, Rachel; Dause, Richard; Perkins, Walter R.; Janoff, Andrew S.  
 CS The Liposome Company, Inc., Princeton Forrestal Center, One Research Way, Princeton, NJ, 08540-6619, USA  
 SO Biochimica et Biophysica Acta, Biomembranes (1997), 1329(2), 370-382  
 CODEN: BBBMBS; ISSN: 0005-2736  
 PB Elsevier B.V.  
 DT Journal  
 LA English  
 AB Incorporation of N-( $\omega$ -carboxy)acylamido-phosphatidylethanolamines (-PEs) into large unilamellar vesicles (LUVs) of L- $\alpha$ -distearoylphosphatidylcholine (DSPC) was found to dramatically increase the in vivo liposomal circulation lifetime in rats, reaching a maximal effect at 10 mol.% of the total phospholipid. Neither pure DSPC liposomes nor those with the longest circulating derivative, N-glutaryl-dipalmitoylphosphatidylethanolamine (-DPPE), were found to significantly bind complement from serum. Therefore, the relatively short circulation time of pure DSPC liposomes did not appear to be related to greater complement opsonization leading to uptake by the reticuloendothelial system. However, N-( $\omega$ -carboxy)acylamido-PEs were particularly efficient inhibitors of a limited aggregation detected for pure DSPC liposomes. The aggregation tendency of DSPC liposomes incorporating various structural analogs of N-glutaryl-DPPE correlated inversely with the circulation lifetimes. Therefore, it is concluded that such PE derivs. enhance the circulation time by preventing liposomal aggregation and avoiding a poorly understood mechanism of clearance that is dependent on size but is independent of complement opsonization. At high concns. of N-glutaryl-DPPE (above 10 mol.%), the liposomes exhibited strong complement opsonization and were cleared from circulation rapidly, as were other highly neg. charged liposomes. These data demonstrate that both the lack of opsonization and the lack of a tendency to aggregate are required for long circulation. Liposomal disaggregation via N-( $\omega$ -carboxy)acylamido-PEs yields a new class of large unilamellar DSPC liposomes with circulation lifetimes that are comparable to those of sterically stabilized liposomes.  
 IT 123689-62-3P  
 RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)  
 (liposomal aggregation vs. complement opsonization in enhancement of circulation lifetime of L- $\alpha$ -distearoylphosphatidylcholine liposomes)  
 RN 123689-62-3 CAPLUS  
 CN 9,11,15-Trioxa-6-aza-10-phosphahentriacontanoic acid, 10-hydroxy-5,16-dioxa-13-[(1-oxohexadecyl)oxy]-, 10-oxide (9CI) (CA INDEX NAME)



RE.CNT 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 17 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN  
 AN 1997:231302 CAPLUS  
 DN 126:282815  
 TI Reduction of liposome-induced adverse physiological reactions  
 IN Ahl, Patrick L.; Bhatia, Suresh K.; Minchey, Sharma R.; Janoff, Andrew S.  
 PA Liposome Co., Inc., USA  
 SO U.S., 29 pp., Cont.-in-part of U.S. Ser. No. 207,651, abandoned.  
 CODEN: USXXAM

DT Patent  
 LA English

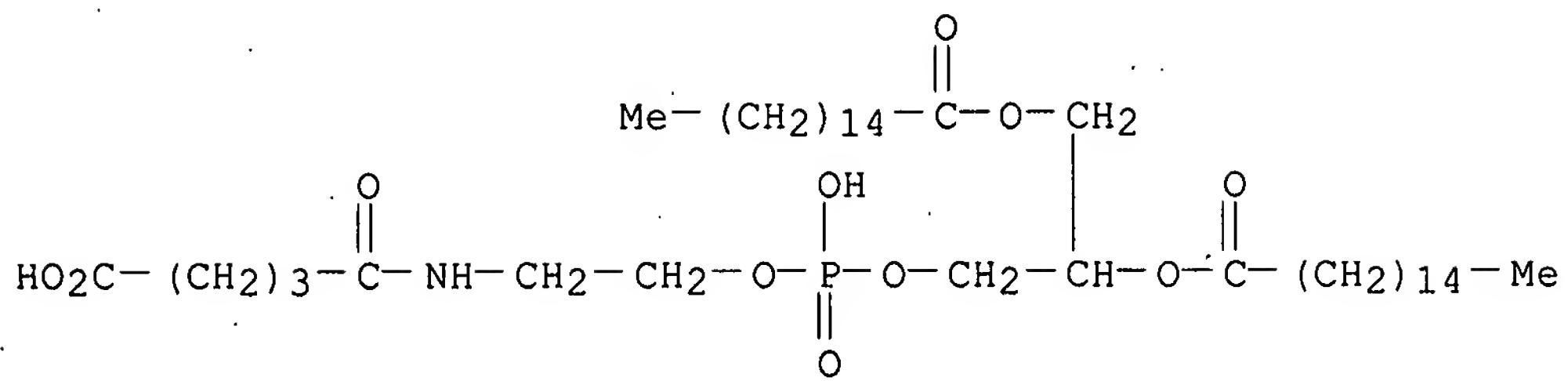
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5614214	A	19970325	US 1994-247053	19940520
	CA 2160118	A1	19941208	CA 1994-2160118	19940520
	EP 1118326	A2	20010725	EP 2001-100692	19940520
	EP 1118326	A3	20020731		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE ES 2165875	T3	20020401	ES 1994-918106	19940520
	PT 699068	T	20020628	PT 1994-918106	19940520
	US 5662930	A	19970902	US 1995-433665	19950504
PRAI	US 1993-65928	B2	19930521		
	US 1994-207651	B2	19940307		
	EP 1994-918106	A3	19940520		
	US 1994-247053	A3	19940520		

AB The blood pressure decrease associated with administering bioactive agent-containing liposomes to an animal is diminished by incorporation into the liposomes (diameter 200-5000 nm) of a phosphatidylethanolamine conjugated to a dicarboxylic acid in such amount that this conjugate comprises  $\geq 10\%$  of the liposome's bilayer. Thus, distearoylphosphatidylcholine liposomes were prepared which contained 5 mol% dipalmitoylphosphatidylethanolamine-glutaric acid conjugate.

IT 123689-62-3P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (reduction of liposome-induced adverse physiol. reactions)

RN 123689-62-3 CAPLUS  
 CN 9,11,15-Trioxa-6-aza-10-phosphahentriacontanoic acid, 10-hydroxy-5,16-dioxo-13-[(1-oxohexadecyl)oxy]-, 10-oxide (9CI) (CA INDEX NAME)



L13 ANSWER 18 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1996:404755 CAPLUS

DN 125:67758

TI Ether lipid liposomes for cancer treatment

IN Mayhew, Eric; Janoff, Andrew S.; Ahmad, Imran; Bhatia, Suresh K.

PA Liposome Company, Inc., USA

SO PCT Int. Appl., 45 pp.

CODEN: PIXXD2

DT Patent

## LA English

FAN.CNT 7

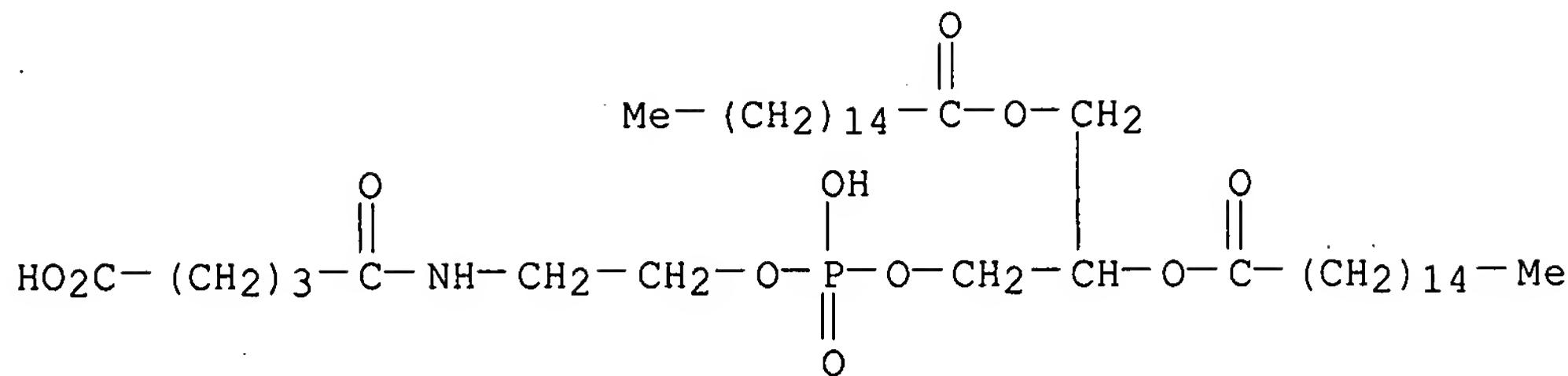
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9611670	A1	19960425	WO 1995-US12721	19951012
W: AU, CA, FI, JP, KR, NO				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2199179	A1	19960425	CA 1995-2199179	19951012
AU 9537625	A	19960506	AU 1995-37625	19951012
AU 707414	B2	19990708		
EP 785773	A1	19970730	EP 1995-935710	19951012
EP 785773	B1	20010103		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10507450	T	19980721	JP 1996-513281	19951012
AT 198419	T	20010115	AT 1995-935710	19951012
ES 2153053	T3	20010216	ES 1995-935710	19951012
PT 785773	T	20010531	PT 1995-935710	19951012
FI 9701494	A	19970410	FI 1997-1494	19970410
NO 9701643	A	19970609	NO 1997-1643	19970410
NO 316206	B1	20031229		
GR 3035689	T3	20010731	GR 2001-400538	20010402
PRAI US 1994-323042	A	19941014		
WO 1995-US12721	W	19951012		
OS MARPAT 125:67758				
AB Ether lipids R1OCH2CH(ZR2)CH2R3 [R1 = Y1Y2; Y1 = CH3, CO2H; Y2 = alkopolyenyl; Z = O, S; R2 = Y1Y2, (fluoro)alkyl; R3 = R5P(O)(OH)OR6; R5 = O, S, NH; R6 = CH2CH2N+Me3, CH2CH2NH2, CH2CH(OH)CH2OH, CH2CH2NHC(O)R7; R7 = Y2CH3, Y2CO2H] are incorporated into liposomes with a headgroup-derivatized lipid (e.g. a phosphatidylethanolamine-dicarboxylic acid) and optionally a sterol and a neutral lipid for treatment of cancer and inflammatory diseases. These liposomes have low hemolytic, hepatotoxic, and enterotoxic activities. Thus, the ether lipid, 1-O-octadecyl-2-O-methyl-sn-glycero-3-phosphocholine, incorporated into phosphatidylcholine/cholesterol/phosphatidylethanolamine-glutaric acid liposomes, inhibited growth of human A549 lung cancer cells in vitro and inhibited metastasis of Lewis lung cancer in mice.				

IT 123689-62-3

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(ether lipid liposomes for cancer treatment)

RN 123689-62-3 CAPLUS

CN 9,11,15-Trioxa-6-aza-10-phosphahentriacontanoic acid, 10-hydroxy-5,16-dioxo-13-[(1-oxohexadecyl)oxy]-, 10-oxide (9CI) (CA INDEX NAME)



L13 ANSWER 19 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1993:567584 CAPLUS

DN 119:167584

TI Specific targeting with polyethylene glycol-modified liposomes: coupling of homing devices to the ends of the polymeric chains combines effective target binding with long circulation times

AU Blume, G.; Cevc, G.; Crommelin, M. D. J. A.; Bakker-Woudenberg, I. A. J. M.; Kluft, C.; Storm, G.

CS Medizinische Biophysik, Urologische Klinik und Poliklinik der Technischen Universitaet Muenchen, Klinikum r.d.I., Munchen, Germany

SO Biochimica et Biophysica Acta, Biomembranes (1993), 1149(1), 180-4  
CODEN: BBBMBS; ISSN: 0005-2736

PB Elsevier B.V.

DT Journal

LA English

AB One possibility for bringing drugs to their specific targets is to use the drug-laden liposomes that have been made target-specific by the attachment of appropriate proteins. Such 'directed' proteoliposomes and most other particles are rapidly removed from the bloodstream, however, by the mononuclear phagocytes in the liver and spleen. This causes suboptimal drug accumulation at the target site. Coating the liposome surface with polyethylene glycol (PEG) may prolong the circulation time of liposomes. Using plasminogen as a homing device the authors have shown that the PEG-modified liposomes with such a homing device coupled to the ends of the long PEG chains may combine long vesicle circulation times in the blood with high target binding capability. The PEG-coated proteoliposomes with homing devices attached at the very bilayer surface, on the contrary, are long-lived but have only little or no capability to bind to their targets.

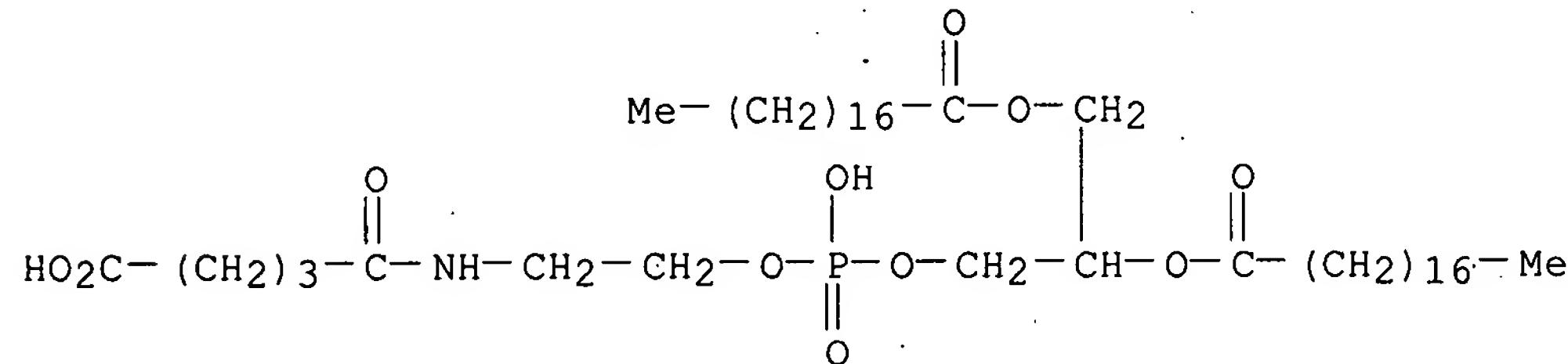
IT 150150-68-8

RL: BIOL (Biological study).

(liposomes containing, PEG-modified, for target binding with long circulation time)

RN 150150-68-8 CAPLUS

CN 9,11,15-Trioxa-6-aza-10-phosphatritriacontanoic acid, 10-hydroxy-5,16-dioxo-13-[(1-oxooctadecyl)oxy]-, 10-oxide (9CI) (CA INDEX NAME)



L13 ANSWER 20 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN

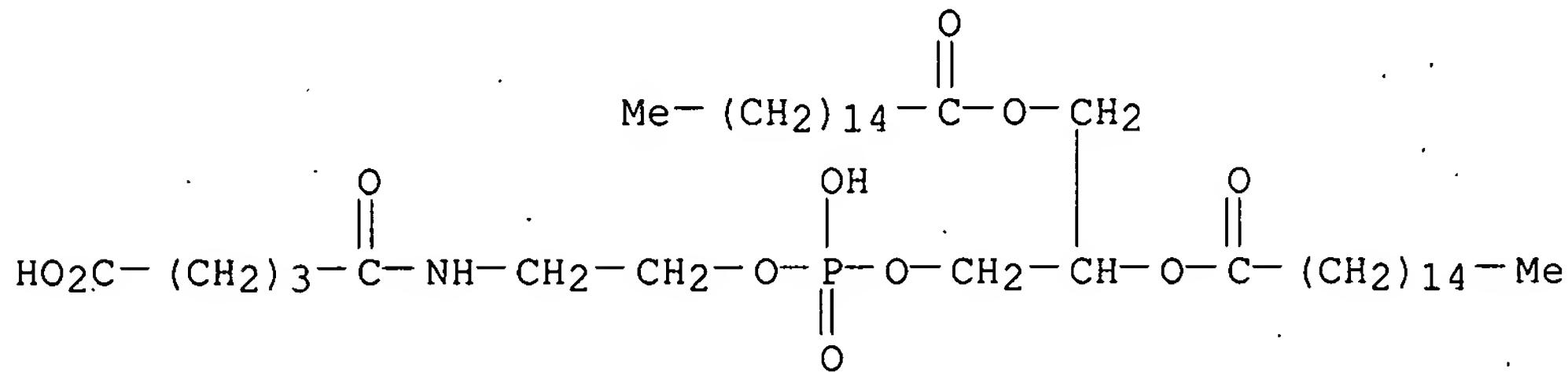
AN 1991:627813 CAPLUS  
 DN 115:227813  
 TI Carboxyacyl derivatives of phospholipid, and carbodiimide method for sensitizing liposome with antigen or antibody for liposome lysis immunoassay  
 IN Umeda, Mamoru; Kobayashi, Reiji  
 PA Nissui Seiyaku Co., Ltd., Japan  
 SO Jpn. Kokai Tokkyo Koho, 7 pp.  
 CODEN: JKXXAF  
 DT Patent  
 LA Japanese  
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 03073856	A	19910328	JP 1989-209789	19890814
PRAI JP 1989-209789		19890814		

AB Carboxyacyl derivs. of phospholipid are used to introduce antigen or antibody to the surface of liposome which encapsulates a hydrophilic label for liposome lysis immunoassay for diagnosing endocrine disease. With the liposome, the immunoassay is simple and sensitive, and is not influenced by complement interference, i.e. antigen-antibody complex formation-independent lysis. Thus, N-succinyl, glutamyl, adipoyl, pimeloyl, suberyl, sebacyl, (11-carboxyimidecanoyl), and (13-carboxytridecanoyle) dipalmitoylphosphatidylethanolamine were prepared from dipalmitoyl phosphatidylethanolamine and succinic; glutaric; adipic; pimelic; suberic; sebacic; decadicarboxylic; and dodecanedicarboxylic anhydrides, and were used to link anti-C-reactive protein (CRP) IgG with liposome by adding ethyldimethylpropylaminocarbodiimide. The IgG sensitized liposome was then used for CRP determination in human blood.

IT 123689-62-3P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of, for sensitizing liposome with antigen or antibody via carbodiimide, for preventing complement interference in liposome lysis immunoassay)

RN 123689-62-3 CAPLUS  
 CN 9,11,15-Trioxa-6-aza-10-phosphahentriacontanoic acid, 10-hydroxy-5,16-dioxo-13-[(1-oxohexadecyl)oxy]-, 10-oxide (9CI). (CA INDEX NAME)



L13 ANSWER 21 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN  
 AN 1989:610777 CAPLUS  
 DN 111:210777  
 TI Interaction of erythrocyte plasma membranes with "gel" liposomes (neutral and negatively charged)  
 AU Bel'tser, N. V.; Anishchuk, M. G.; Bogdanov, A. A., Jr.; Torchilin, V. P.  
 CS A. V. Palladin Inst. Biochem., Kiev, USSR  
 SO Biologicheskie Membrany (1989), 6(9), 955-65  
 CODEN: BIMEE9; ISSN: 0233-4755  
 DT Journal  
 LA Russian  
 AB Interactions of human erythrocytes with gel-phase liposomes prepared from dipalmitoylphosphatidylcholine (DPPC) or from DPPC and

N-glutaryl-dipalmitoylphosphatidylethanolamine mixture (9:1 molar ratio) were studied by transmission electron microscopy. The data obtained suggest the following dynamics of liposome-erythrocyte membrane interactions: in contrast to neutral liposomes, neg. charged ones rapidly bind to the cell surface (in the presence of 2 mM CaCl<sub>2</sub>); their membranes immediately undergo destabilization concomitant with glycocalyx elimination from the areas of close contact between liposome and erythrocyte membranes. Then liposomal lipids incorporate into the cell membrane causing echinocytic shape transformations followed by particle release from the tips of spicules. The erythrocyte membrane and cytoskeletal proteins seem to play a major role in the liposome-cell interactions. Treatment of erythrocytes with crosslinking agents before incubation with liposomes does not prevent binding of liposomes to the cell surfaces but strongly inhibits further mixing (fusion) of lipid components of the contacting membranes.

IT 123689-62-3  
RL: BIOL (Biological study)  
(liposomes containing, cell membrane of human erythrocytes interaction with gel-phase)  
RN 123689-62-3 CAPLUS  
CN 9,11,15-Trioxa-6-aza-10-phosphahentriacontanoic acid, 10-hydroxy-5,16-dioxo-13-[(1-oxohexadecyl)oxy]-, 10-oxide (9CI) (CA INDEX NAME)

